

A thesis submitted in partial fulfilment of  
the requirements for the degree of  
Doctor of Philosophy in the discipline of Physiotherapy

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AN ASSESSMENT OF NEUROMUSCULAR  
PERFORMANCE, FUNCTIONAL RANGE OF  
MOTION AND QUALITY OF LIFE  
CHARACTERISTICS IN CHILDREN  
DIAGNOSED WITH HYPERMOBILITY  
SYNDROME

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A thesis submitted in partial fulfilment of the  
requirements for the degree of Doctor of  
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## ABSTRACT

**Introduction:** Hypermobility syndrome (HMS) is a common cause of morbidity in children, with the knee most frequently affected by its symptoms. Impaired joint proprioception has been reported in adults with HMS. Muscle weakness, problems with school activities and abnormal gait patterns have been observed in children with this condition. It has also been suggested that activities of daily living and physical and sporting activities may be limited in children with HMS due to pain. To date, the factors associated with HMS in children have not been well reported. The relationships between impairments, function and quality of life (QoL) have not been investigated in children with this condition. The purpose of this study was to identify the range of neuromuscular performance, functional range of motion (ROM) and QoL indices, and investigate the relationships between these features in children with HMS. A purpose-built motorised device was developed and validated for the assessment of knee joint proprioception as an integral part of the research programme. The test-retest repeatability of various outcome measures used for the present study was also investigated in healthy children and those with HMS.

**Methods:** A cross-sectional study was conducted. Twenty nine children with HMS and 37 healthy children (aged 8 – 15 years) were investigated for neuromuscular indices, functional ROM and QoL. Knee joint kinaesthesia (JK) and position sense (JPS) were examined using a motorised device, muscle torque was tested with a digital myometer, passive ROM was measured with a universal goniometer and functional ROM was assessed using the VICON camera system. Pain intensity and QoL were measured using the Coloured Analogue Scale and the Paediatric Quality of life Inventory respectively. Mann-Whitney U tests and independent t-tests were performed to determine the differences between the two groups. The relationships between pain and each of the following: neuromuscular impairments, functional ROM and QoL were examined in children with HMS. The correlation between Beighton scores and each outcome was also evaluated in children with HMS.

**Results:** Knee JK and JPS were significantly poorer (both  $p < 0.001$ ) in children with HMS compared with the controls. Significantly reduced ( $p < 0.001$ ) knee muscle torque was also observed in children with HMS. Pain intensity and passive knee ROM were significantly higher (both  $p < 0.001$ ) in children with HMS. They also demonstrated significantly increased knee extension, reduced knee flexion in loading response and during maximal knee flexion of walking (all  $p < 0.001$ ). Moreover, the overall QoL perception and all the domains were significantly poorer ( $p$  range  $< 0.001$  to  $0.008$ ) in children with HMS than the controls. No relationship ( $r$  range =  $-0.065$  to  $0.271$ ;  $p$  range =  $0.106$  to  $0.985$ ) was found between pain, neuromuscular impairments and functional ROM in children with HMS. However, a significantly strong negative relationship ( $r = -0.65$ ;  $p = < 0.001$ ) was established between pain and QoL in children with HMS. In addition, no relationship ( $r$  range =  $-0.014$  to  $0.315$ ;  $p$  range =  $0.112$  to  $0.895$ ) was observed between Beighton scores and neuromuscular impairments, functional ROM and QoL in children with HMS.

**Conclusions:** Children with HMS, compared with their healthy counterparts had knee joint proprioception and knee muscle torque deficits, increased passive knee ROM and pain intensity. Abnormal walking patterns (increased knee extension, reduced knee flexion in both mid stance and maximum knee flexion in swing phase during walking) were also found in children with HMS. They also presented with poorer QoL in comparison with the controls. Clinicians are to be aware of these identified features and should develop appropriate treatment intervention programmes for children with this condition.

**Keywords:** Hypermobility syndrome, proprioception, impairments, functional ability and quality of life

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## **ABBREVIATIONS**

AAE: Absolute angular error  
ACL: Anterior cruciate ligament  
ADL: Activities of daily life  
AEV: Angular error of variation  
APPT: Adolescent paediatric pain tool  
AROM: Active range of motion  
ASIS: Anterior superior iliac spine  
BOD: Body outline diagram  
BHMS: Benign hypermobility syndrome  
BS: Beighton score  
CAS: Coloured analogue scale  
CMD: Craniomandibular disorder  
CNS: Central nervous system  
CP: Cerebral Palsy  
CPM: Controlled passive movement  
CROM: Cervical range of motion  
DMD: Duchenne muscle dystrophy  
EDS: Ehlers Danlos syndrome  
ELGON: Electrogoniometer  
EMG: Electromyography  
ET: Extensor thrust  
FAP: The Functional Ambulation Profile  
FIM: Functional Independence Measure  
FSIIR: Functional Status II Revised  
FTD: Fixed torque device  
GCA: Geometric centre axis  
GJL: Generalised joint laxity  
HHD: Hand held dynamometer  
HHM: Hand held myometer  
HMAL: Human Motion Analysis Laboratory  
HMS: Hypermobility syndrome  
HRQOL: Health related quality of life  
IASP: International Association for the Study of Pain  
ICF: International Classification of Functioning, Disability and Health

ICC: Intraclass correlation coefficient  
IQR: Interquartile range  
JK: Joint kinaesthesia  
JPS: Joint position sense  
KAD: Knee alignment device  
KFLR: Knee flexion loading response  
KEMS: Knee extension in mid-stance  
LCL: Lateral collateral ligament  
LOA: Limits of agreement  
MCL: Medial collateral ligament  
MDF: Medium density fibre  
MKF: Maximum knee flexion  
MMT: Manual muscle testing  
OA: Osteoarthritis  
PCL: Posterior cruciate ligament  
PedsQL: Paediatric quality of life questionnaire  
PPM: Pearson's product moment correlation  
PROM: Active range of motion  
PVC: Polyvinyl chloride  
QMU: Queen Margaret University  
QoL: Quality of life  
RA: Rheumatoid Arthritis  
RAE: Relative angular error  
RCT: Randomised control trial  
RHSC: Royal Hospital for Sick Children  
ROM: Range of movement  
SD: Standard deviation  
SPSS: Statistical Package for Social Sciences  
TEA: Transepicondylar axis  
TMJ: Temporomandibular joint  
UK: United Kingdom  
USA: United States of America  
VAS: Visual analogue scale  
VE: Visual estimation

# **CHAPTER 1 : INTRODUCTION**

## **1.1 Background to the Study**

Hypermobility syndrome (HMS) was defined by Kirk et al. (1967) as a generalised joint laxity (GJL) with associated musculoskeletal complaints in the absence of any systemic rheumatic diseases. Joint laxity is an increased mobility of small and large joints beyond the range of motion considered normal (Biro et al. 1983). GJL is a condition in which most synovial joints possess greater range of motion than normal limits (Boyle et al. 2003). The aetiology of GJL and HMS is unknown, although GJL is a prime feature of HMS and it is believed that it is genetic disorders of collagen fibres (Grahame et al. 1999). This thesis specifically deals with HMS with referrals to GJL being made only in recognition of its contribution to HMS.

The prevalence of GJL in preschool children has been reported to be as high as 64.6% (Lamari et al. 2005). In children, GJL decreases with increasing age (Cheng et al. 1991; Jansson et al. 2004) and girls are found with a higher degree of GJL than boys at any age (Jansson et al. 2004; Seckin et al. 2005; Bird 2007). GJL may incur no ill effects in children (Grahame et al. 1999; Engelbert et al. 2003; Engelbert et al. 2006) and may be an advantage in some sports, such as ballet dancing (McCormack et al. 2004). However, HMS, sometimes called benign hypermobility syndrome (BHMS), is diagnosed when GJL becomes symptomatic with musculoskeletal complaints in the absence of signs of any rheumatic, neurologic, skeletal, or metabolic disorders (Engelbert et al. 2005). It is a common complaint in paediatric rheumatology and among healthy school children (Biro et al. 1983). HMS accounted for 26% of referrals to the paediatric rheumatology clinic at the Royal Hospital for Sick Children (RHSC), Edinburgh (Kerr et al. 2000) of which most had knee and/or ankle complaints. The reported prevalence of HMS may vary according to the criteria and cut-off points used for assessment (Cherpel and Marks 1999) as there is no universally accepted 'gold standard' for defining GJL and HMS.

It has been suggested that children with HMS may present with a variety of neuromusculoskeletal complaints such as joint pain, muscle pain, back pain and muscle weakness (Maillard and Murray 2003). The knee joint is most commonly affected by the symptoms of HMS in children (Everman and Robin 1998; Kerr et al. 2000; Adib et al. 2005). The only well-reported complaints affecting children with this

condition are multiple joint pains (Everman and Robin 1998). Apart from joint pain, the first neurophysiological dysfunction reported in adults with HMS was impaired joint proprioception (Mallik et al. 1994; Hall et al. 1995). To date, joint proprioception has not been investigated in children with this condition.

Knee joint proprioception is commonly assessed using motorised devices (Barrack et al. 1983a; 1983b; Skinner et al. 1984; Skinner et al. 1986; Grob et al. 2002; Robert et al. 2003; Xu et al. 2004). Joint kinaesthesia (JK) and joint position sense (JPS) are two techniques commonly used for testing proprioception of the knee joint (Barrack et al. 1983c; Corrigan et al. 1992; Grob et al. 2002). These two proprioceptive tests have been shown to elicit different responses in the same group of subjects (Fridén et al. 1997). Moreover, in adults, a lack of correlation has been observed between the two tests (Grob et al. 2002). It is currently unknown whether, in children, similar disparities are evident in the relationship between the two techniques. There is limited information regarding knee joint proprioception in children, as only one study was found investigating this in children using a motorised device (Barrack et al. 1983c). This may be due to lack of a quantitative method of assessing this outcome in children. Therefore, there was a need for a motorised device to be developed for assessing knee joint proprioception in healthy children and those with HMS.

Adults with HMS have also been found with neuromusculoskeletal signs such as carpal and tarsal tunnel syndromes (Francis et al. 1987; March et al. 1988), and symptoms of sciatica (Beighton et al. 1989). Autonomic (Gazit et al. 2003) and musculoskeletal reflex (Ferrell et al. 2007) dysfunctions have recently been reported in association with HMS in adults, which further confirms that there may be some neuromuscular impairments in patients with HMS. Despite the common occurrence of HMS in children and increasing knowledge of neuromuscular impairments in adults with this condition, little attention has been given to its clinical implications in children. Therefore, it is unknown whether children with HMS present with similar neuromuscular impairments.

Some researchers (Jaffe et al. 1988; Tirosh et al. 1991) have reported that gross and fine motor development may be delayed in children with GJL. On the other hand, investigators such as Davidovitch et al. (1994) and Engelbert et al. (2005) reported no relationship between GJL and fine motor development in children. The above-mentioned authors examined children with GJL and not those with HMS their results may not therefore be applicable to children with HMS. Muscle weakness has been reported in adults with HMS (Sahin et al. 2007). In addition, it is believed that muscle weakness around lax joints (Biro et al. 1983), particularly of the lower limbs (usually in the knee) may be a feature of HMS in children (Maillard and Murray 2003). However, cross-sectional studies by Engelbert et al. (2003; 2004; 2006) revealed no significant difference in 'total muscle strength' between children with HMS and healthy controls. In the above three studies by Engelbert et al., the sample sizes were small, limiting the generalisability of their findings. In addition, the knee, which is mostly affected by the symptoms of HMS (Kerr et al. 2000; Adib et al. 2005), was not examined in their studies.

Some years ago, it was suggested that individuals with HMS may present with abnormal joint biomechanics due to ligamentous laxity (Hall et al. 1995; Grahame 2000a), however, this view is yet to be confirmed empirically. Only a few authors have investigated gait characteristics in children with HMS (Engelbert et al. 2004; Adib et al. 2005). Toe-walking was seen in children with HMS by Engelbert et al. (2004) suggesting that children with this condition may present with abnormal gait patterns. This was corroborated by Adib et al. (2005) who observed abnormal gait patterns and delayed walking in these children. However, the precise nature of gait abnormality in these children was not investigated by Adib et al. It is therefore uncertain whether abnormal knee joint biomechanics are found in children with HMS during walking.

Anxiety, panic attacks, and phobias (Bulbena et al. 1993) have been observed in adults with this condition. In a study of adults with HMS by Ferrell et al. (2004) a significant improvement in quality of life (QoL) and other neuromuscular parameters was reported following an 8-week exercise programme. It is not clear whether QoL was poorer in individuals with HMS than their healthy counterparts, however, due to a lack of a parallel control group in Ferrell et al.'s study.



It has been suggested that activities of daily living and physical and sporting activities may be limited in children with HMS due to pain (Gurley-Green 2001; Murray and Woo 2001). However, Ruperto et al. (2004) investigated functional ability and physical and psychosocial well-being of school children with GJL and those without GJL. They found that none of these were significantly affected in children with GJL. In addition, Ruperto et al. (2004) reported that children with GJL had role and social limitations compared with those without GJL. These studies were not conducted on children with HMS, therefore, it is unknown whether QoL is affected in these children.

Many diagnostic criteria have been developed for GJL and HMS. These include the Carter and Wilkinson scoring system (1964), Beighton et al. (1973), Bulbena et al. (1992) and Brighton criteria (Grahame 2000a) and Comtompasis scoring system (Poul and Fait 1986). The Beighton score (in the presence of pain) is frequently used to diagnose HMS as they could be applied by clinicians in a few minutes (Bird 2005). They have recently been validated in Dutch children (van der Giessen et al. 2001). They are described as a set of crude diagnostic joint movements (Grahame 1990) designed for epidemiological studies (Bulbena et al. 1992). The Beighton method does not consider some joints that may also become symptomatic such as the shoulder joint. In addition, this method does not give the extent of laxity at specific joints and indicate the severity of symptoms found in HMS (Grahame 1999).

Diagnosis of HMS using any of the above mentioned criteria (based on measuring passive range of movement and musculoskeletal pain) has some limitations. The observed range of movement using the criteria depends on the force applied to the moving part (Engelbert et al. 2005). In addition, the presensnce of pain may not be sufficient to reflect the range of other possible factors (such as neuromuscular impairments, functional ability and QoL characteristics) in children with this condition.

It is believed that HMS is under-recognised and sometimes dismissed as a pathological condition (Grahame and Bird 2001) therefore children with HMS are often not identified during clinical assessment (Lewkonja and Ansell 1983; Grahame 2000a). Even though children with HMS are occasionally referred for physiotherapy (Engelbert et al. 2005) their condition has no definitive treatment (Ferrell et al. 2004)

and therefore they may not receive appropriate intervention (Lewkonja and Ansell 1983; Grahame 2000b).

At present, there is no general agreement on which neuromuscular indices are affected in children with HMS as most previous studies have focused on adults (Mallik et al. 1994; Hall et al. 1995; Sahin et al. 2007). To date, the relationships between neuromuscular indices have also not been reported in children with HMS. The author of this thesis is also not aware of any study that has investigated the effect of neuromuscular impairments on functional ability and or QoL in children with HMS. There is currently a lack of indepth knowledge of the factors associated with this condition in children.

The influence of age and gender on these indices in healthy children has also not been well documented. If clinicians are to successfully manage children with HMS, the knowledge of the factors associated with their condition is important. This study addressed the need to develop an understanding of the neuromuscular performance, functional ROM and QoL characteristics in both healthy children and those with HMS. This investigation also examined the relationships between these characteristics in children with this condition.

## **1.2 Aims of the Study**

The aims of the present study are divided into primary and secondary.

### **1.2.1 Primary Aims**

1. To identify the neuromuscular performance, functional ROM and QoL characteristics in children diagnosed with HMS and healthy children.
2. To determine the relationships between pain and each of the following: proprioception, muscle torque, passive ROM, functional ROM (during walking) and QoL in children diagnosed with HMS.

### **1.2.2 Secondary Aims**

1. To develop and validate a motorised device for assessing knee joint proprioception.
2. To determine the test-retest/intra-rater repeatability of methods for assessing the neuromuscular performance, functional ROM and QoL characteristics in healthy children and those diagnosed with HMS.

3. To investigate the effect of gender and age on neuromuscular, functional ROM and QoL indices in healthy children.
4. To determine the relationship between knee JK and JPS in healthy children.

This research focussed on the knee joint for the following reasons:

1. The knee joint appears to be mostly affected by symptoms of HMS (Everman and Robin 1998; Kerr et al. 2000; Vougiouka et al. 2000; Adib et al. 2005).
2. Previous studies on joint proprioception in adults with HMS were conducted on the knee (Hall et al. 1995; Ferrell et al. 2004); hence, their findings were available for comparison with the results of the current investigation.

### **1.3 Outline of Thesis**

Chapter 1 has discussed the 'Background to the study and Aims of the study'.

Chapter 2 describes the 'Aetiology/Pathophysiology, Epidemiology and Clinical Features of Generalised Joint Laxity/HMS' in Children'.

Chapter 3 reviews the 'Diagnostic Criteria for Generalised Joint Laxity and HMS, and Methods of Assessing Associated factors'. This review focuses on the different diagnostic criteria used for generalised joint laxity and HMS, and instrumented method of assessing ROM. Different methods of assessing pain, muscle strength, functional ROM during walking and QoL are also reviewed.

Chapter 4 describes 'Joint Proprioception' beginning with different definitions of proprioception, neurophysiology of proprioception, a summary of the structure and function of proprioceptors, factors affecting joint proprioception, and methods of assessing joint proprioception. The relationship between joint kinaesthesia (JK) and joint position sense (JPS) are also examined. In addition, different types of JPS measurement errors are described.

Chapter 5 presents the 'Equipment Development and Validation'. The criterion-related validity of lower leg displacement when placed in the limb support of the motorised device, within-day repeatability of JPS test and between-days repeatability of marker placement are also reported in this chapter.

Chapter 6 contains 'Test-retest Repeatability of the Outcome Measures for Evaluating Neuromuscular Impairments, Functional ROM during walking and QoL characteristics in healthy children and children with HMS'.

Chapter 7 describes the 'Assessment of Healthy Children and those Diagnosed with HMS'. Experimental design, subject recruitment and sample size determination are also presented. This chapter discusses ethical considerations and approval, inclusion/exclusion criteria, experimental procedure and data analysis. The 'Results of the Assessment of Healthy Children and those with HMS are also presented in this chapter which include the following: neuromuscular impairments, functional ROM during walking and QoL characteristics in healthy children and those with HMS, the effect of gender and age on these characteristics in healthy children, and relationship between knee JK and JPS in healthy children. In addition, the relationships between pain and each measurement parameter and between Beighton scores and each of the outcomes examined in children with HMS are described.

Chapter 8 'Discussion'. The findings in both children with HMS and healthy controls are discussed. Clinical implications of the findings are also examined.

Chapter 9 contains 'Summary, Conclusions and Recommendations' of the present research including the strengths and limitations. Suggestions for future studies are also highlighted.

## **1.5 Summary of Chapter One**

From the foregoing, it is clear that HMS affects a sizeable proportion of children. The neuromuscular performance, functional ROM and QoL characteristics associated with HMS are not known. In addition, the relationships between these characteristics in children with this condition are yet to be understood. These may impact on the treatment received by children with HMS. Therefore, the primary aims of the current research are to identify the neuromuscular performance, functional ROM and QoL characteristics in children with HMS and determine the relationships between them.

The next chapter presents the aetiology/pathophysiology and epidemiology of GJL/HMS in children. The clinical features of HMS as they relate to neuromusculoskeletal impairments, activity limitations and participation restrictions are also discussed.

## **CHAPTER 2 : AETIOLOGY, EPIDEMIOLOGY AND CLINICAL FEATURES OF GENERALISED JOINT LAXITY AND HYPERMOBILITY SYNDROME IN CHILDREN**

### **2.1 Introduction**

The terms '*generalised joint laxity*' and '*joint hypermobility*' are often used interchangeably. In addition, the terms '*hypermobility syndrome*', '*joint hypermobility syndrome*' and '*benign joint hypermobility syndrome*' are also sometimes used interchangeably. Because of the ambiguity, the terms '*generalised joint laxity*' (GJL) and '*hypermobility syndrome*' (HMS) are used throughout in this thesis.

The aetiology of GJL, as well as the long-term outcome of children with this entity is unknown (Tirosh et al. 1991). The primary cause of GJL is increased ligamentous laxity (Maillard and Murray 2003; Bird 2005). Ligamentous laxity is inherent in a person's make up and it is determined by the influence of fibrous protein genes, in particular those that encode collagen, elastin, and fibrillin (Grahame 1999). GJL may also result from joint destruction in diseases such as rheumatoid arthritis (Klemp 1997). Diseases such as hyperparathyroidism and rheumatic fever are also thought to predispose to GJL (Beighton et al. 1989; Klemp 1997).

GJL is thought to be a disorder of the connective tissue (Grahame 2000a; Hakim et al. 2004). It may be a feature of hereditary disorders of the connective tissues such as Marfans syndrome (an autosomal dominant disorder of the connective tissues) and Ehlers-Danlos syndrome (a heterogeneous group of heritable disorders of the connective tissue, characterised by skin extensibility, generalised joint laxity and tissue fragility). GJL is also found in rare disorders of amino acid metabolism, and it may exist as an acquired condition in some neurological and rheumatic diseases (Milkkelsson et al. 1996). Other factors such as sex hormones (Calguneri et al. 1982), occupation and training or repetitive activities (Klemp et al. 1984) may predispose to joint laxity. GJL seems to be inherited as a gender-influenced dominant feature which is more common in girls than boys (Biro et al. 1983; Klemp et al. 1984; Larsson et al. 1987; Jasson et al. 2004; Seckin et al. 2005; Bird 2007).

GJL may be a risk factor for musculoskeletal complaints such as pain in four or more joints longer than three months, dislocation in more than one joint or in one joint on more than one occasion, and soft tissue rheumatism with  $\geq 3$  lesions (e.g. epicondylitis, tenosynovitis, bursitis). According to Bird (2007), the following may also be found in HMS: 1). Marfanoid habitus (tall, slim, span:height ratio  $>1.03$ , upper:lower segment ratio  $<0.89$ , arachnodactyly); 2). Abnormal skin (striae, hyperextensibility, thin skin, papyraceous scarring); 3). Eye signs (drooping eyelids or myopia or antimongoloid slant); and 4). Varicose veins, hernia or uterine/rectal prolapse. Therefore, HMS is diagnosed when GJL becomes symptomatic or associated with some of the above factors in the absence of any rheumatic disease. The primary clinical feature found in association with GJL is multiple joint pain. Patients with HMS may also present with neuromusculoskeletal signs such as impaired joint proprioception (Mallik et al. 1994; Hall et al. 1995).

This chapter provides an overview of the possible causes and factors predisposing to GJL and HMS. The epidemiology and clinical features of HMS (relating to impairments, activity limitations and participation restrictions) are also discussed in this chapter.

## **2.2 Aetiology of Generalised Joint Laxity and HMS**

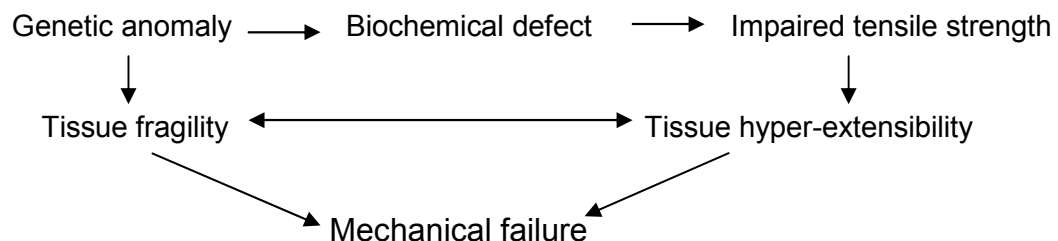
### **2.2.1 Generalised Joint Laxity**

Generalised joint laxity (GJL) is believed to be due to abnormality of type I collagen (Child 1986). Type I collagen is the most common collagen in the human body (Maillard and Murray 2003). With a high tensile strength, type I collagen is normally abundant in connective tissues such as tendons, ligaments, joint capsules, skin, demineralised bone and nerve receptors (Prockop and Kivirikko 1995; Maillard and Murray 2003). Type II collagen is found primarily in hyaline cartilage (Maillard and Murray 2003), and type III collagen in the same tissues as type I collagen, usually in lesser amounts (Prockop and Kivirikko 1995). Type III collagen compared with types I and type II collagen is thin and elastic. It is found in greater amounts in extensible connective tissues (vascular system, skin and lung) (Prockop and Kivirikko 1995). The ratio of type III collagen to type III + I collagen (III: III + I) was found to increase in individuals with HMS (Handler et al. 1985; Child 1986). Normally, this ratio is 18%: 21%, whereas in people with HMS this ratio was found to be 28%: 46% (Handler et al. 1985). Electron microscopy of skin biopsies showed that these

individuals had a decreased number of thick collagen fibres and increased prevalence of fine disorganised fibres when compared with age-matched controls (Handler et al. 1985). Therefore the decreased tissue stiffness (increased joint laxity) seen in children with GJL may be the result of the abnormal ratio of collagen types (Handler et al. 1985).

### 2.2.2 Hypermobility Syndrome (HMS)

The mechanism by which joint symptoms develop in individuals with HMS is not well understood. However, it may be related to excessive stretching of ligaments (Gedalia et al. 1993). The joints are normally surrounded by soft tissues: joint capsule, ligaments, tendons and muscles (Gedalia et al. 1993). These structures are responsible for joint stability (Maillard and Murray 2003). Excessive motion or inappropriate physical activities that hyperextend the joints, stretches the capsules, ligaments and other soft tissues causing micro-trauma (Gedalia et al. 1993; Everman and Robin 1998). In addition, joint instability resulting from ligamentous laxity (Maillard and Murray 2003) due to abnormality of collagen fibres (Bird 2005) may also lead to soft-tissue micro-trauma (Gedalia et al. 1993). It is also believed that stresses on a lax joint of individuals with GJL may lead to biomechanically disadvantaged loading conditions being adopted by the joint and this may result in micro-trauma (Lewkonia and Ansell 1983). Pain in children with HMS is also believed to occur because of enhanced tissue sensitivity or recent sprain/strain injuries (Adib et al. 2005). Joint laxity in HMS may lead to wear and tear of the joint surfaces, impose stresses on a joint and predisposes the sufferer to premature articular degeneration (Lewkonia and Ansell 1983). As shown in Figure 2.1, Grahame (2000b) suggested that there is a strong relationship between genetic abnormality, biomechanical defect and mechanical consequences in individuals with HMS.



**Figure 2.1: The relationship between genetic anomaly, biomechanical defect and mechanical consequences (adapted from Grahame 2000b).**



Complaints in HMS may also be due to fragility of the collagen (Bulbena et al. 1992) providing inadequate support to a joint. Over-stimulation of sensory nerve endings and primary muscular defects may also be the causes of joint and muscle pain seen in children with HMS (Beighton et al. 1989; Gedalia et al. 1993).

The increased incidence of acroparesthesia (abnormal neurological sensation of one or more extremities) reported in individuals with HMS (El-Shahaly and E-Sherif, 1991) is thought to be due to abnormalities in the nerve tissue as well as surrounding connective tissues. Impaired joint proprioception (Mallik et al. 1994; Hall et al. 1995) may be due to damage to joint receptors from the excessive mobility of their joints, which might explain the apparent tendency to experience ligament and joint capsule trauma (Grahame 2000a) due to impaired sensory feedback from the affected joint.

### **2.2.3 Summary**

In summary, GJL may be caused by ligamentous laxity. This is inherent in a person's make up and is determined by the influence of their fibrous protein genes. Of particular importance in this respect are the genes that encode collagen, elastin, and fibrillin. GJL may also be associated with irreversible changes that occur in connective tissues in certain acquired diseases including acromegaly and hyperparathyroidism.

The factors contributing towards the development of HMS seem to be complex. They may be damage to joint receptors from excessive joint mobility, or inappropriate physical activities that hyperextend the lax joint and stretches the capsules, ligaments and other soft tissues, causing micro-trauma and over-stimulation of nerve endings.

In the next section, the epidemiology of GJL and HMS in children will be discussed.

## **2.3 Epidemiology**

### **2.3.1 Generalised Joint Laxity in Children**

Children possess an inherent greater range of motion in their joints than adults, with a gradual reduction in this range observed with age. GJL is classified into pauci-articular (or localised) and poly-articular (Larsson et al. 1987). Pauci-articular by definition is when less than five joints are involved whereas poly-articular is when five or more joints are involved (Grahame 1999).

Table 2.1 summarises the prevalence of GJL in children. At the moment there is no general agreement on the prevalence of GJL. Table 2.1 illustrates that GJL can be seen in up to 64.6 % of the children (Lamari et al. 2005), depending on the criteria used to define it. GJL has been reported to decrease with age (Cheng et al. 1991; Larsson et al. 1993b; Jansson et al. 2004) as joints tend to stiffen and lose mobility. The pauci-articular variety has been reported to be more prevalent (Grahame 1999). In general, Table 2.1 shows that the overall prevalence of GJL in children ranges from 8.8% to 64.6%. It also demonstrates that GJL affects girls more than boys of the same age. From the Table it can be seen that the prevalence of GJL ranged from 3.3% to 60% in boys and 10.8 to 68.8% in girls. Decorster et al. (1997) found that the incidence of GJL in adolescent athletes was greater in girls than in boys at a ratio of 4:1. Qvindesland and Jonsson (1999) demonstrated that the prevalence of HMS in Icelandic 12-year-olds was higher in girls than in boys at a ratio 3:1. GJL is believed to be more prevalent among younger females of Asian, African and Middle Eastern populations (Finsterbush and Podrond 1982; Larsson et al. 1993; Everman and Robin 1998).

Given the high prevalence of GJL in children, it is possible that a large proportion of these children may develop symptoms associated with HMS.

**Table 2.1: Summary of some studies reporting the prevalence of generalised joint laxity in children**

<b>Authors</b>	<b>Criteria used (cut off point)</b>	<b>Age (years)</b>	<b>Sample size &amp; Population</b>	<b>Number of Boys/ Girls</b>	<b>Total Prevalence (%)</b>	<b>Prevalence in Boys (%)</b>	<b>Prevalence in Girls (%)</b>
Gedelia et al. (1985)	Beighton (not reported)	5 - 17	260 American school children	134/126	12.3	6.7	18.3
Forleo et al. (1993)	Beighton ( $\geq 5/9$ )	5 - 17	1005 Brazilian school children	445/589	36.3	41.1	58.9
Subramanyan and Janaki (1996)	Beighton ( $\geq 4/9$ )	6 - 15	1000 South Indian children	500/500	17.2	19.1	15.0
Decoster et al. (1997)	Beighton ( $\geq 5/9$ )	Mean 15.5	364 US adolescent athletes	150/114	12.9	6.9	33.7
Vougiouka et al. (2000)	*Beighton ( $\geq 3/5$ )	5 - 14	2432 Greek school children	1280/1152	8.8	7.1	10.8
Seckin et al. (2005)	Beighton ( $\geq 4/9$ )	13 - 19	861 Turkish high school students	428/433	11.7	Not reported	Not reported
Lamari et al. (2005)	Beighton ( $\geq 4/9$ )	4 - 7	1120 Brazilian preschool children	534/586	64.6	60	68.8
Gyldenkerne et al. (2007)	Beighton ( $\geq 4/9$ )	12 - 13	364 Danish grammar school children	178/156	9.4	3.3	16.6

\*measured only the right limbs and lumbar flexion.

### **2.3.2 Hypermobility Syndrome in children**

The prevalence of GJL and how it is affected by gender, age and ethnic background has been discussed in section 2.3.1. In this section the prevalence of HMS in children is examined. It is believed that most children with GJL have no ill effects and enjoy a symptom-free life (Engelbert et al. 2005). Beighton et al. (1989) reported that children with HMS usually present with complaints after the age of 10 years and only occasionally before the age of 5. Table 2.2 and 2.3 present a summary of the studies that have reported the prevalence of joint/muscle pain in school children and HMS among paediatric rheumatology referrals respectively. From Table 2.2 it can be seen that the prevalence of pain among school children with GJL ranged from 30% to 55%. In Table 2.3, it can be observed that the prevalence of HMS among paediatric referrals was 5.7% to 26%. The data reported on the prevalence rate should be regarded with caution because of the following reasons: 1. Different criteria and cut off points were used by the authors; 2. Children of different ages were studied and this may therefore have affected their findings as it has been shown that GJL decreases with age (Larsson et al. 1993); 3. Participants in the studies presented in Tables 2.2 and 2.3 were recruited from different populations (Paediatric rheumatology referrals and school children) with variable sample size; 4. The inclusion and exclusion criteria and how participants were recruited were not stated in some cases. Despite these limitations, the following conclusions could be drawn from Tables 2.2 and 2.3: a. It appears that the knee joint is most commonly affected by the symptoms of HMS; b. HMS seems to be a common condition in children with rheumatological conditions; c. A large proportion of children with GJL might also present with the symptoms of HMS.

**Table 2.2: The prevalence of joint pain/muscle pain among school children with generalised joint laxity**

<b>Authors</b>	<b>Criteria used (cut off point)</b>	<b>Age (years)</b>	<b>Sample size &amp; Population</b>	<b>Number with GJL</b>	<b>Number with pain</b>	<b>Total (%) with pain</b>
Arroyo et al. (1988)	Beighton ( $\geq 5/9$ )	5 – 19	192 American school children	Not reported	66	34
Mikkelsen et al. (1996)	Beighton ( $\geq 6/9$ )	Mean 3 <sup>rd</sup> grade = 9.8; Mean 5 <sup>th</sup> grade = 11.8	1637 Finish school children in 3 <sup>rd</sup> and 5 <sup>th</sup> grades	127	38	29.9
El-Garf et al. (1998)	Beighton ( $\geq 4/9$ )	6 – 15	997 Egyptian school children	116	35	30
Qvindenland and Jónsson (1999)	Beighton ( $\geq 4/9$ )	12	267 Icelandic school children	74	41	55

**Table 2.3: The prevalence of HMS in children with rheumatological conditions**

<b>Authors</b>	<b>Criteria used (cut off point)</b>	<b>Age (years)</b>	<b>Sample size &amp; Population</b>	<b>Number with HMS</b>	<b>Total (%) with HMS</b>	<b>Joints affected</b>	<b>Joint affected most</b>
Biro et al. (1983)	Beighton ( $\geq 3/5^*$ )	Not reported	262 Paediatric rheumatology referrals	15	5.7	Knees, hands & fingers	Knee
Kerr et al. (2000)	Beighton (not reported)	2 -14	Paediatric rheumatology referrals. Sample size not reported	51 children diagnosed with HMS	26% of paediatric rheumatology referrals	Knee, ankle	Knee
De Inocencio et al. (2004)	Beighton ( $\geq 4/9$ )	4 - 14	222 paediatric referrals	43	19.4	Not stated	Not reported
Adib et al. (2005)	Beighton (not reported)	< 18	Paediatric referrals to rheumatology and hypermobility clinics. Sample size not reported	189 children with HMS	Not reported	Knee, elbow, ankle etc	Knee

Key:

\*measured only the right limbs and lumbar flexion.

### **2.3.3 Conclusion**

The prevalence of GJL may be up to 64.6% in children (Lamari et al. 2005) and the occurrence of joint/muscle pain among school children with GJL can be as high as 55% (Qvindesland and Jónsson 1999). In addition, the prevalence of HMS among paediatric rheumatological referrals may be as high as 26% (Kerr et al. 2000). GJL also varies among ethnic groups and decreases with increase in age. GJL appears to be more common in girls than boys.

In the majority of the epidemiological studies, the authors did not state the inclusion and exclusion criteria for their studies and how their study participants were recruited. The samples used in most of these studies were small. Therefore, their results may not reflect the true prevalence of GJL and HMS in children. Despite these limitations, these studies provide some useful information for future research.

The anatomy and biomechanics of the knee joint in the following section examines.

## **2.4 Anatomy and Biomechanics of the Knee Joint**

Table 2.3 demonstrated that the knee joint is mostly affected by the symptoms of HMS. Therefore, for a good understanding of the joint, issues relating to the biomechanics of the knee joint are discussed in this section. The knee is primarily a hinge type of synovial joint. The components of this joint include a bicondylar femur, cruciate ligaments, and menisci. The knee accepts, transfers, and dissipates often high loads among the femur, tibia, patella and fibula (Dye 1996; Dye et al. 1998). It is believed that the knee joint cannot function normally without the complex neurological components providing sensory innervation (including proprioception) as well as active muscle control (Dye and Vaupel 2000). Detailed description of the anatomy, motor and sensory innervations of the knee joint are provided by Moore and Dalley (1999) and Dye and Vaupel (2000). The mechanisms and neurophysiology of proprioception are dealt with in more detail in chapter 4 of this thesis. The following section describes the biomechanics and flexion-extension axis of the knee joint.

### **2.4.1 Biomechanics and axis of the Knee Joint**

The knee joint is formed by the femur and tibia. In addition, the patella lies within the patella tendon and glides over a groove on the front of the femur during knee motion. The main movements of the knee joint are flexion and extension. However, some rotation occurs when the knee is flexed (Moore and Dalley 1999). When the knee is fully extended with the leg and foot on the ground the knee locks because of medial rotation of the femur on the tibia. This makes the lower limb a solid column and more adapted for weight bearing (Moore and Dalley 1999).

The knee joint axis for flexion-extension ROM is commonly described using two axes (Most et al. 2004): the transepicondylar axis (TEA), which connects the most prominent points on the lateral and medial condyles (Churchill et al. 1998) and the geometric centre axis (GCA) that is defined as a line connecting the centres of the two femoral condyles (Li et al. 2004). Geometrically, differences have been observed between these two axes (Eckhoff et al. 2001; Li et al. 2004). Churchill et al. (1998) found that TEA closely approximates the optimal flexion-extension axis of the knee joint. Eckhoff et al. (2004) observed that GCA represents a single, fixed axis for flexion-extension at the knee joint. However, tibia rotation using the GCA was significantly higher ( $p < 0.05$ ) than TEA throughout the entire range of knee flexion (Most et al. 2004).

Although the TEA represents an accurate axis for estimating flexion-extension ROM at the knee joint, it is not truly fixed as it changes throughout the ROM (Snyder-Macker and Lewek 2006). This change is believed to be due to the incongruence of the joint surfaces. The large articular surface of the femur and the small tibia condyle create a potential problem as the femur begins to flex on a fixed tibia. When knee flexion ( $0^{\circ}$  to  $25^{\circ}$ ) is initiated, the femoral condyles roll on the tibia, bringing them in contact with the tibia condyle posteriorly (Snyder-Macker and Lewek 2006). With further knee flexion, the rolling of the femoral condyles is accompanied by anterior glide that creates a spin of the femur on the posterior tibia with linear displacement of the femoral condyles after  $25^{\circ}$  of knee flexion. Knee extension from flexion is a reversal of this motion. When the tibia flexes on a fixed femur, for example during a seated position such as when knee joint proprioception is tested, the tibia both rolls and glides posteriorly on the relatively fixed femoral condyles. However, anterior roll and glide of the tibia occur when the tibia is extended on a



fixed femur. Detailed information on the knee biomechanics is provided by Snyder-Macker and Lewek (2006).

Lehmkuhl and Smith (1983) believed that changing in the axis of motion of the human knee during flexion-extension movement causes problems when devices with mechanical hinge joints such as a goniometer, isokinetic dynamometer and proprioception devices are applied to the knee joint. It has been observed that when the knee joint is moved the anatomical axis of the joint moves, while the mechanical axis of the aligned device remains fixed (Lehmkuhl and Smith 1983). Therefore, the ROM of the knee may differ at different phases of movement. Acknowledging this limitation, the TEA method has been used to define flexion-extension axis during goniometry measurement (Clarkson 2000; Norkin and White 2003) and knee proprioception assessment (Dvir et al. 1988; Marks 1994; Macdonald et al. 1996; Tsang and Hui-Chan 2003; Tsang and Hui-Chan 2004; Xu et al. 2004). In addition the TEA, readily identifiable (Churchill et al. 1998; Most et al. 2004) can be found in all knees (Yoshiho et al. 2001) and has been found to be highly repeatable (Beger et al. 1993; Nagamine et al. 1998; Suter et al. 2006). Given these reasons, the TEA was used as the flexion-extension axis of the knee joint in the present study.

The following section examines the clinical features that may be associated with HMS.

## **2.5 Clinical Features**

In section 2.3 it was concluded that HMS affected a considerable proportion of healthy children and those with rheumatological conditions. It is believed that many children show evidence of GJL, but only a small percentage may present with musculoskeletal complaints (Beighton et al. 1989; Grahame 2000a; Engelbert et al. 2005). These complaints may occur at any age and their severity will vary from child to child (Beighton et al. 1989). The most prominent features found in individuals with HMS are neuromusculoskeletal signs such as pain (Everman and Robin 1998) and muscle weakness (Adib et al. 2005).

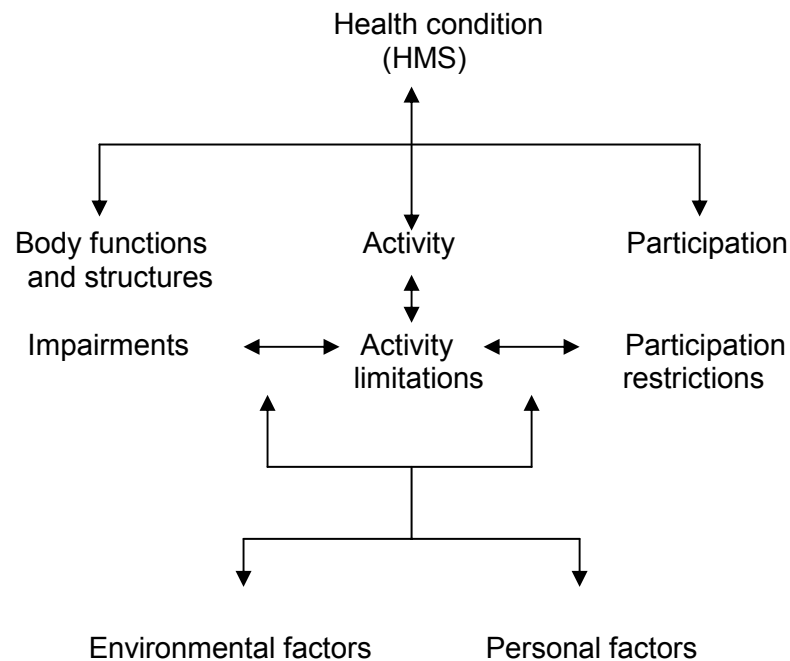
Non-articular symptoms have also been found in individuals with HMS (El-Shahaly and El-Sherif 1991). For example, Grahame et al. (1981) reported an increased incidence of mitral valve prolapse in patients with HMS. Varicose veins (El-Shahaly et al. 1991) have also been found in individuals with HMS. In addition, rectal (Marhman et al. 1987) and uterine (Al-Rawi et al. 1982) prolapses were found in association with HMS. Bulbena et al. (1993) established a significant association between GJL and anxiety states including panic attacks and phobic states. Children with HMS are believed to be generally unfit and have very poor stamina (Maillard and Murray 2003). From the foregoing, it is clear that HMS causes problems to children at three levels: impairment, activity limitation and participation restriction (WHO 2001). In order to select the appropriate outcomes that reflect these three levels, the International Classification of Functioning, Disability and Health (ICF) model was used.

### **2.5.1 The International Classification of Functioning, Disability and Health (ICF)**

The primary goal of physiotherapy treatment of patients with musculoskeletal disorders is to restore optimal functioning (Jette 1993). It is believed that optimal functioning of an individual includes all body functions, activities and participation (WHO 2001). Physiotherapy assessment and treatment of children with HMS are mostly based on impairments such as ROM or pain. Researchers have suggested that activity limitations and participation restrictions may also be found in children with this condition (Gurley-Green 2001; Murray and Woo 2001). However, neuromusculoskeletal impairments and the extent to which they contribute to activity limitations and participation restrictions have not been well reported in children with HMS. In order to identify and evaluate the consequences of health problems on

functional activities and participation, the World Health Organisation developed the ICF (Kjeken et al. 2005).

The ICF (Figure 2.2) is made up of three main domains, body structure/function, activity and participation (Harris et al. 2005) called the positive aspects. Problems areas within the domains are called impairments, activity limitations and participation restrictions which are referred to as the negative elements. These domains can be affected by environmental and personal factors also known as contextual factors (Stucki and Ewert 2005). The ICF framework can be used to classify the impact of health (Harris et al. 2005) and select appropriate outcome measures by physiotherapists (Mayston 2007). Studies have linked outcome measures to the ICF domains to better reflect all aspects of health outcomes in patients with musculoskeletal conditions (Harris et al. 2005).



**Figure 2.2: The World Health Organisation ICF (Adapted form Stucki and Cieza 2004; Stucki and Ewert 2005; Mayston 2007).** The ICF provides a useful tool to examine impairments, activity and participation of the child with musculoskeletal condition and serves as a useful framework for intervention. The upper half of the figure indicates the positive elements (e.g function) and the lower half shows the negative (e.g participation restrictions).

The specific elements of the framework are defined as follows:

**Impairments:** Deficits in physiological or anatomical structures in relation to a disease condition. Examples are pain, muscle weakness, reduced proprioception and ROM (Harris et al. 2005)

**Activity limitations:** These are difficulties an individual has in performing a task or action. An example is difficulty in walking (Stucki and Ewert 2005; Kjekken et al. 2005).

**Participation restrictions:** The problems that an individual may experience in engaging in life situations such as roles and activities (Harris et al. 2005). These may be reflected in QoL assessment.

**Personal factors:** These are contextual factors that relate to the individual such as age, gender, social status and life experience (Stucki and Ewert 2005).

**Environmental factors:** External or extrinsic factors of an individual person's life which impact on her/his functioning such as attitude and values, social systems and services, policies and laws (Stucki and Ewert 2005).

In the present study outcomes were selected based on the dimensions of ICF model (Kjekken et al. 2005; Mayston 2007). The following measures were chosen to reflect the impairment variables: pain (Kjekken et al. 2005), ROM (Harris et al. 2005; Kjekken et al. 2005), muscle strength (Kjekken et al. 2005) and proprioception (Hurley et al. 1997). Activity limitation was measured using functional ROM during walking (Stucki and Ewert 2005). Quality of life (QoL) was chosen as a measure of participation restriction (Jette 1993; Harris et al. 2005). Therefore, the terms '*impairments*', '*activity limitations*' and '*participation restrictions*' will be used in the present work to classify the features associated with HMS in terms of the ICF.

The most commonly investigated symptom associated with HMS in children is pain. It is unknown at the moment if other neuromuscular impairments (such as joint proprioception and muscle strength) are also found in children with HMS. Therefore the focus of the present research was on impairments due to the number of measures at this level and because little is known at this basic level. The research also focussed on activity limitations (functional ROM) and participation restrictions (QoL) in children with HMS. Only the symptoms relating to these factors (neuromuscular impairments, activity limitations and participation restrictions) are discussed in this thesis. These possible features are summarised in Table 2.4. Due to the limited published data on these symptoms of HMS in children and because most studies have focussed on adults, studies carried out in adults with this condition are also examined in this chapter.

In the next section, neuromusculoskeletal signs of HMS are examined.

**Table 2.4: Summary of neuromuscular, musculoskeletal, gait abnormality and quality of life features associated with GJL and HMS**

<b>Authors</b>	<b>Population</b>	<b>Clinical Feature(s)</b>
Grahame et al. (1981), Grahame (2000b)	-	Pars interarticularis defects, spondylolisthesis
Finsterbugsh and Pogrund (1982)	-	Joint dislocations
Pitcher and Grahame (1982)	Patients with MVP	Back pain
Francis et al. (1987)	11 patients	Peripheral neuropathy and HMS
Rajapakse et al. (1987)	Patients with MVP	Fractures, joint dislocations
Jaffe et al. (1988)	729 infants aged 8 to 14 months	Delayed motor development
March et al. (1988)	-	Carpal tunnel syndrome
Westling (1989); Perrini et al. (1997)	-	TMJ dysfunction
El-Shahaly and El-Sherif (1991)	-	Soft tissue rheumatism, carpal and tarsal tunnel syndromes
Bridges et al. (1992)	Participants included those with HMS, connective tissue disorders and fibromyalgia	Scoliosis
Bulbena et al. (1993)	-	Anxiety disorders
Diaz et al. (1993)	Studied population made up of male soldiers	Musculotendinous lesion

Keys:

MVP = Mitral valve prolapse

TMJ = Temporomandibular joint

HMS = Hypermobility syndrome

**Table 2.4 (Continued): Summary of neuromuscular, musculoskeletal, gait abnormality and quality of life features associated with Generalised Joint Laxity and HMS**

<b>Authors</b>	<b>Population</b>	<b>Clinical Feature(s)</b>
Davidovitch et al. (1994)	Children with HMS	Delayed walking
Mallik et al. (1994); Hall et al. (1995)	Adults with HMS	Impaired proprioception
Hudson et al. (1995); Grahame (2000b)	-	Epidcondylitis
Al-Rawi and Nessian (1997)	-	Anterior knee pain
Bulbena et al. (1988); Bulbena et al. (1993); Martin-Santos et al. (1998)	Adults with GJL.	Panic attacks
El-Garf et al. (1998)	-	Pes planus
Gazit et al. (2003)	Adults with HMS	Autonomic reflex dysfunction
Engelbert et al. (2004)	-	Toe-walking
Engelbert et al. (2004)	children with HMS	Exercise induced pain
Adib et al. (2005)	Children with HMS	Abnormal walking pattern
Ferrell et al. (2007)	Adults with HMS	Muscle weakness
Sahin et al. (2007)	Adults with HMS	Musculoskeletal reflex dysfunctions

Keys:

GJL = Generalised joint laxity; HMS = Hypermobility syndrome

MVP = Mitral valve prolapse; TMJ = Temporomandibular joint

### **2.5.2 Neuromusculoskeletal Signs of HMS**

There are many neuromusculoskeletal signs that may be associated with GJL and HMS as detailed in Table 2.4. Pain is the most common sign reported in children with HMS (Biro et al. 1983; Everman and Robin 1998). Pain may be localised in one joint or it may be generalised and symmetrical. Lewkonia and Ansell (1983) reported that large and medium sized joints were more frequently affected than small joints. According to Grahame (1990), joint complaints in children with HMS are self-limited in duration. They may recur with strenuous physical activities (Gedalia and Brewer 1993; Everman and Robin 1998) and tend to occur later in the day following strenuous physical activities (Beighton et al. 1989; Grahame 1990; Everman and Robin 1998). In contrast to arthritic conditions, morning stiffness is an uncommon finding in these children (Everman and Robin 1998). Physical examination may also reveal pain upon joint movement, which may be accompanied with mild degrees of effusion in the absence of signs of active inflammation such as significant tenderness, swelling, redness, warmth, and fever (Everman and Robin 1998). The neuromusculoskeletal signs previously reported in individuals (adults and children) with HMS are discussed below.



**Table 2.5: Studies reporting knee joint problems in individuals diagnosed with HMS**

<b>Authors</b>	<b>Diagnostic criteria and cut off point used</b>	<b>Sample size and age</b>	<b>Joint (s) affected most</b>	<b>Population</b>
Finsterbush and Pogrund (1982)	Carter & Wilkinson. Cut off point not reported	100 patients: 51 females and 14 males	Knee	Age of participants not reported
Lewkonja and Ansell (1983)	Carter & Wilkinson. Cut off point not reported	54 children: 42 girls and 12 boys; Age range = 2 – 16 years.	Knee	-
Hudson et al. (1995)	Beighton. $\geq 4/5$	46 adults: Mean age 45.5; Age range = 16 – 72 years	Spine (thoracic and low back)	Study participants included adults with HMS
Kerr et al. (2000)	Beighton. Cut off point not reported	39 children: Age range = 2 – 14 years	Knee and ankle	A retrospective study, Knee alone accounted for 26% of symptomatic joints.
Vougiouka et al. (2000)	*Beighton. $\geq 3/5$	189 children: Age range = 5 – 14 years	Knee	Parents completed questionnaire regarding their children's musculoskeletal complaints
Adib et al. (2005)	Beighton. Cut off point not reported	125 children aged < 18 years	Knee	Data collected both prospectively and retrospectively

Key:

\*measured only the right limbs and lumbar flexion.

### **2.5.2.1 Pain**

Pain is believed to be a common reason for referring children with HMS for examination and treatment in paediatric practice (Lewkonia nad Ansell 1993; De Inocencio 2004). Due to limited information on pain experience in children with HMS, studies in adults with HMS are also included in the literature review in this section to attempt to determine relevant information.

Laxity of the knee joint is considered as a possible predisposing factor to the development of anterior knee pain (Al-Rawi and Nessian 1997). Pain often develops after strenuous physical activities or sports, during which the affected joint(s) is/are, used repeatedly (Everman and Robin 1998). In a study by Biro et al. (1983) 262 children diagnosed with HMS and referred to a paediatric arthritis clinic (over a period of 2½ years) were studied. Pain and/or swelling of various joints were found to be the usual complaints. Pain was found to occur more frequently between the ages of 10-15 years. The most common sites of complaints were the knees and the fingers. Similarly, joint pain was found in 74% of 125 children diagnosed with HMS aged <18 years (Adib et al. 2005). They also observed that the knee joint accounted for 66% of the complaints in these patients. The distribution of pain in individuals with HMS is illustrated in Table 2.5.

Russek (2000) observed that recurrent multiple-joint pain (involving the feet, ankles, hips, shoulders, wrists and fingers) was associated with HMS in a 28-year-old woman. The patient's pain experience, examined with a visual analogue scale, was reported to have been felt at end range movements of the joints. The observation by Russek cannot be generalised as only one patient was investigated in that study.

On the other hand, a lack of association between GJL and musculoskeletal complaints has been reported (Mikkelsen et al. 1996). These authors examined 1637 primary school children (mean age  $10.9 \pm 1.1$  years) using a pre-tested structured questionnaire to assess musculoskeletal symptoms. GJL was determined using a Beighton score of  $\geq 6$  and children were asked to complete the questionnaire. The occurrence of musculoskeletal pain was found to be about the same in children with GJL (29.9%) and those without GJL (32.3%). It is unknown whether some children examined had HMS or not as the inclusion and exclusion criteria in that study were not clearly stated, therefore it can be argued that the

findings reported by Milkkelsson et al. may be because healthy school children with GJL were examined and not those with HMS.

At the moment, there is limited published data on pain experience in children with HMS. It also appears that there is conflicting evidence regarding pain experience in children with this condition. In order to investigate pain intensity in children with HMS, future studies are required. Therefore, this provided justification for the assessment of pain experience in children diagnosed with HMS in the current study.

#### **2.5.2.2 Joint Proprioception**

Proprioception, as defined by Voight et al. (1996, p. 348) “is the cumulative neural input to the central nervous system from specialised nerve endings called mechanoreceptors”. These mechanoreceptors are found in the joint capsules, ligaments, muscles, tendons and skin (Voight et al. 1996; Hurley et al. 1998). Proprioception requires processing of sensory information from these peripheral mechanoreceptors, vision and vestibular system (Hurley et al. 1998). Joint kinaesthesia (JK) and joint position sense (JPS) are components of proprioception. Garn and Newton (1988) described JK as the conscious awareness of joint position and movement, resulting from proprioceptive input to the central nervous system. JPS defined by Corrigan et al. (1992, p. 247), is the “awareness of a joint in space.” Proprioception is important for normal function in activities of daily living, occupational tasks and sports (Skinner et al. 1986; Borsa et al. 1994).

Following an extensive literature search only three studies (Mallik et al. 1994; Hall et al. 1995; Ferrell et al. 2004) were found that have investigated joint proprioception in adults with HMS. However, no study was found by the author of this thesis on joint proprioception in children with HMS. Since GJL (in the absence of any rheumatic disease) is a feature of HMS, the studies found on proprioception in adults with both HMS and those with GJL are examined in this section.

Mallik et al. (1994) studied 12 women with HMS (mean age 29 years) and 12 healthy (women mean age 29 years). HMS was defined by the presence of a Beighton score of  $\geq 4/9$  and musculoskeletal pain. These authors discovered impairment in proprioception acuity at the proximal interphalangeal joint of the HMS patients compared with the controls ( $p = 0.0001$ ). The findings of Mallik et al. (1994) provide preliminary data on joint proprioception in patients with HMS, however, the

knee joint (believed to be most commonly affected by the symptoms of HMS) was not examined in their study.

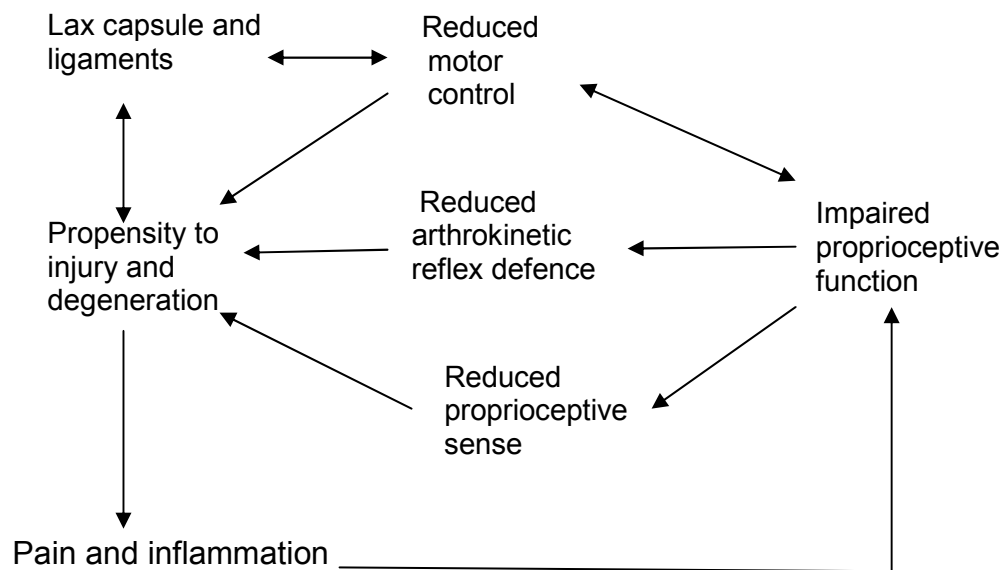
In another study by Hall et al. (1995), 10 women with HMS (mean age 30.3 years) were examined for knee JK. The control group were made up of male (mean age 29.7 years) and female (mean age 30.0 years) subjects. They reported that knee JK was significantly ( $p < 0.001$ ) poorer in women with HMS compared with the age and gender matched controls. Although the knee joint was examined by Hall et al. (1995), however, only JK (a component of joint proprioception) was investigated hence their finding may not represent the overall proprioceptive acuity in patients with HMS. In addition, adults with HMS were examined and study therefore their observation cannot be extrapolated to children.

Barrack et al. (1983a) investigated passive JPS of the knee joint in a study of 12 ballet dancers (men and women; mean age 25 years) with GJL and a group of 12 active healthy controls (men and women; mean age 24 years). They found a significant impairment ( $p < 0.03$ ) in knee JPS in the ballet dancers compared with matched controls. Similarly, Blasier et al. (1994) demonstrated significantly impaired knee JK in healthy men and women with knee joint laxity. 34 subjects (mean age  $\pm$  SD =  $19.6 \pm 1.5$  years) participated in the study. Rozzi et al. (1999) also reported a significantly less sensitive JK of the shoulder in 29 subjects with GJL (age range 20 to 42 years). Additionally, diminished knee JPS at end-range extension in 24 women (mean age  $24 \pm 3$  years) with standing genu recurvatum was also reported by Loudon (2000). In the above-mentioned studies (Barrack et al. 1983a; Blasier et al. 1994; Rozzi et al. 1999; Ludon 2000) healthy adults with joint laxity were examined. Therefore, their findings cannot be extended to children diagnosed with HMS.

Stillman et al. (2002) investigated knee joint laxity and JPS in 44 healthy young men and women. All study participants had a history of active participation in regular sports spanning more than 5 years. Subjects' test limbs were passively moved to the test angle following which they were asked to actively reproduce the angle. Better proprioceptive acuity was observed in subjects with greater knee joint mobility compared to those with less knee joint mobility ( $p = 0.03$ ). It is believed that exercise training enhances joint proprioception (Petrella et al. 1997). It was not stated in Stillman et al.'s study whether individuals with greater joint mobility engaged in

physical activity more than those with less knee mobility. Therefore, the observed findings may be due to the level of physical activity of the participants.

The possible relationships between joint laxity and impaired proprioception are illustrated in Figure 2.3. Mallik et al. (1994) proposed two possible mechanisms that may be responsible for impaired joint proprioception in individuals with HMS. Firstly damage to joint receptors due to joint laxity and secondly, generalised deficit in proprioceptor activation associated with ligamentous laxity. These may account for a decrease in joint afferent firing in subjects with HMS and those with GJL.



**Figure 2.3: Possible links between joint laxity and abnormal proprioception (adapted from Stillman et al. 2002).** Damage to proprioceptors (in the lax ligaments and capsule) causes reduced motor control and predisposes to further joint injury which eventually leads to impaired joint proprioception.

Available evidence shows that joint proprioception may be impaired in adults with HMS. Previous studies have also demonstrated that joint proprioception is impaired in adults with GJL. However, to date no study has investigated this issue in children. Given the findings on joint proprioception in adults with HMS and GJL it is important to determine whether joint proprioception is also impaired in children with HMS. Therefore, the present study was aimed at investigating this issue to find out if the findings of Mallik et al. (1994) and Hall et al. (1995) can be extended to children with HMS.

### **2.5.2.3 Muscle Strength**

Muscle strength is defined as the force exerted by a muscle or group of muscles to overcome a resistance in one maximal effort (Trew and Everett 2001). Muscle helps to give stability to a joint; it controls joint movement and prevents excessive movement (Maillard and Murray 2003). Muscle strength also contributes to the performance of ADL (Hurley et al. 1998; Hughes et al. 1999).

Normal human movement requires sophisticated motor control, adequate muscle strength, smooth pain-free range of motion and strong skeletal support (Amundsen 1990). Muscle strength may be affected by many factors such as pathologies involving upper motor neurons, peripheral nerves, neuromuscular junctions, muscles, and tendons (Amundsen 1990; Norkin and White 2001). Pain, fatigue, and disuse atrophy can also cause muscle strength deficit (Amundsen 1990; Norkin and White 2001). Muscle strength measurements can be used in clinical practice to identify anomalies, set treatment goals and evaluate the effect of intervention (Vermeulen et al. 2005). It is believed that muscle weakness may be a sign of HMS (Middleditch 2003). There is limited information on muscle strength deficit in children with HMS as only three studies have investigated this issue (Engelbert et al. 2003; 2004 and 2006). Therefore, the available literature on muscle strength in both children and adults with HMS are examined in this section.

In a study by Engelbert et al. (2003), 15 children (boys and girls, mean age 8.1 years) with HMS, 16 children with non-symptomatic GJL (mean age 8.9 years) and 79 healthy controls (mean age 9.3 year) were investigated for muscle strength. HMS was defined by the presence of GJL and associated musculoskeletal symptoms such as arthralgia in more than two joints for a period exceeding 12 weeks; exercise-induced pain and intolerance, without the presence of signs of any rheumatic, neurological, skeletal, or metabolic disease (Brighton criteria). Total muscle strength, of shoulder abductors, grip strength, hip flexors and ankle dorsiflexors was measured in that study using a hand-held myometer. Total muscle strength was calculated as the summation of the measurements.

No significant difference was found in the mean total muscle strength (N) reported between the children with HMS and healthy controls. Additionally, no significant difference was observed between children with HMS and those with GJL. However, the mean total muscle strength in Newtons (N) was significantly higher in children with GJL than the healthy controls. The strength of the hamstrings and quadriceps muscles that act on the knee joint (Moore and Dalley 1999) (most commonly affected by the symptoms of HMS Table 2.5) was not examined by Engelbert et al. (2003).

It has also been reported that muscle strength may be affected by many factors such as the moment arm (Smidt and Rogers 1982) and body mass (Keating and Matyas 1996). The moment arm is the perpendicular distance from the line of application of the musculotendinous unit to the axis of rotation for the joint on which the muscles act (Smidt and Rogers 1982). The greater the moment arm, the greater will be the recorded strength of a muscle. Heavier subjects are likely to have artificially higher muscle strength due to the mass of their body segment (Keating and Matyas 1992). These factors were not considered by Engelbert et al. (2003).

Engelbert et al. (2004) found a greater but not statistically significant difference in total muscle strength measured in Newton meters (Nm) in healthy children (mean age 12.8 years) than those with HMS (mean age 11.6 years). These authors examined bilateral total muscle strength of shoulder abductors, hip flexors, ankle dorsiflexors and grip strength using a hand-held myometer. Total muscle strength was calculated as the summation of measurements of shoulder abductors, grip strength, and hip flexors. Their findings may be the result of the protocol used as total muscle strength of five muscle groups was assessed.

Engelbert et al. (2006) also failed to observe a significant difference in muscle strength between healthy children and those with HMS. In their study, the total muscle strength of 282 healthy children and 13 children with HMS was examined by 8 examiners using a hand-held myometer. They acknowledged that the inter-rater repeatability of their measurements was high. However, no reference was made to possible variation in verbal encouragement in their study. It has been shown that verbal encouragement significantly increased muscle torque (McNair et al. 1996);

therefore the lack of significant difference observed in their study may be due to this factor.

The above three studies (Engelbert et al. 2003; 2004 and 2006) have the advantage of being the only investigations found that have examined muscle strength in children with HMS. However, these studies have some limitations. The methods in these studies were not sufficiently detailed to enable precise replication. In addition, the knee, which is the most affected joint by symptoms of HMS (Biro et al. 1983; Everman and Robin 1998; Kerr et al. 2000; Adib et al. 2005), was not examined in those studies. Therefore, it is possible that some of the joints examined were asymptomatic. Moreover, no information was given as to whether children with HMS were undergoing treatment for their condition or not. Giving all these limitations, their findings should be interpreted with caution.

In a study by Sahin et al. (2007) knee extension and flexion muscle strength was examined in 40 adults with HMS (mean age  $\pm$  SD = 27.9  $\pm$  8.1 years) and 45 healthy controls (mean age  $\pm$  SD = 26.7  $\pm$  9.2 year). HMS was diagnosed using the Brighton criteria and muscle strength (of both right and left knee) was examined using an isokinetic dynamometer at three different angular velocities (60, 180 and 240°/s). Statistically significant reduced peak knee extensor muscle strength (p range = 0.005 to 0.045) was observed in the HMS group at the three angular velocities for both limbs. However, only left knee flexion was statistically significant and this was at 60°/s while others were not. The reason for the differing results between knee extension and flexion peak muscle strength is not apparent, however, since adults with HMS were examined the findings may not be applicable to children with HMS.

In a case report, Russek (2000) examined muscle strength using manual muscle testing in a 28-year-old woman diagnosed with HMS. This author reported that the patient's muscles were within normal limits and pain-free throughout the upper and lower extremities. Again only one patient was examined in that study therefore, its findings cannot be generalised.



Ferrell et al. (2004) found a significant improvement in both peak and average strength for both quadriceps and hamstrings ( $p$  range = 0.0002 to 0.038) in 18 adult patients with HMS (mean age  $\pm$  SD = 27.3  $\pm$  10.4 years) following a standardised 8-week home-based closed kinetic exercise programme. It is difficult to draw a definite conclusion on whether the muscles assessed were weaker than in normal as no parallel control group was investigated.

In another study by Ferrell et al. (2007), complete absence of musculoskeletal reflex activity of rectus femoris motoneurons was observed in 7 out of 15 adult patients with HMS. They investigated reflex dysfunction in 15 patients with HMS and 11 age-matched controls. These researchers also found that short latency reflexes were detectable in 100% of the controls, but were completely absent in 47% of the HMS patients ( $p < 0.01$ ). Kirk et al. (1967) and Beighton et al. (1973) observed that most of their HMS patients (children and adults) had poor muscle development. Muscle wasting and weakness have also been found in children with HMS (Adib et al. 2005). It is also believed that decreased muscle bulk may be a feature of HMS as they frequently have a lower muscle tone (Keer and Grahame 2003).

The observations by Kirk et al. (1967); Beighton et al. (1973) and Keer and Grahame (2003) have not been thoroughly investigated. Although there is no direct evidence to suggest that there is a decrease in muscle mass in HMS, it has been postulated that muscle strength deficit may be related to decreased muscle mass (Frontera et al. 1991). A direct significant correlation has also been observed between muscle bulk (cross-sectional area) and muscle strength in children (Kenehisa et al. 1994; 2002). Therefore, combining the postulation of Frontera et al. (1991), the findings of Kenehisa et al. (1994; 2002), the above observations, and findings of Adib et al. (2005), Ferrell et al. (2007) and Sahin et al. (2007), it can be hypothesised that muscle strength deficits may be found in children with HMS compared with controls. A cross-sectional study is needed in children with this condition to confirm whether muscle strength deficit is associated with HMS in children. Thus, muscle strength measurement was also carried out in the present study.

#### **2.5.2.4 Range of Movement (ROM)**

Range of movement (ROM) is commonly examined in children with HMS using the Beighton criteria (Table 3.1). While Beighton criteria are easy to use (Klemp 1984) and they provide a quick indication of GJL (Bird 2005), they are not joint specific and therefore do not give indication of the extent of ROM at specific joints in children with this condition. This limitation makes it difficult for the criteria to be used for monitoring change in ROM in children with HMS. ROM has been quantified in children using universal goniometers (Fairbank et al. 1984; El-Garf et al. 1998) and a fixed torque device (Silman et al. 1987). Only researchers such as Engelbert et al. (2003); Engelbert et al. (2004) and Engelbert et al. (2006) have compared ROM measurements in children with HMS to healthy controls. Although the studies by Engelbert et al. have been discussed previously in this section in relation to muscle strength, these studies will be examined again in respect of ROM. El-Garf et al. (1998) examined elbow and knee joints in healthy school children with a universal goniometer to determine the amount of ROM. However, the specific values of elbow and knee ROM were not reported. Therefore, it is difficult to draw any conclusion from their findings.

Engelbert et al. (2003) found that the 'total passive ROM' at certain joints (shoulder, elbow, wrist, hip, knee and ankle) was significantly higher (95% CI = 154.1<sup>o</sup>, 208.9<sup>o</sup>) in 15 boys and girls with HMS (mean age  $\pm$  SD = 8.1  $\pm$  0.6 years) than 95 healthy children (mean age  $\pm$  SD = 9.2  $\pm$  0.1). A significantly higher ( $p < 0.05$ ) total active ROM at these joints was also observed in 13 children with HMS (mean age  $\pm$  SD = 10.7  $\pm$  2.7) compared with 382 healthy controls (mean age  $\pm$  SD = 14.5  $\pm$  4.0) (Engelbert et al. 2006). In the studies by Engelbert et al. 'total ROM' measured with a universal goniometer was calculated as the summation of all measurements, including that of the knee joint, therefore their findings are not specific to the knee joint.

Engelbert et al. (2004) investigated active knee flexion and extension in 19 boys and girls (aged 11.6  $\pm$  2.7 years) with HMS and 274 healthy controls (aged 12.8  $\pm$  3.3 years). They found that children with HMS had significantly reduced knee flexion ROM and higher knee extension ROM (both  $p < 0.001$ ) compared with healthy controls. Given that joint laxity is a feature of HMS one would expect both knee flexion and extension ROM to be significantly higher in children with HMS than their

healthy counterparts. Their findings may be due to the protocol used for assessing knee ROM (active ROM). Active compared with passive ROM may be limited by knee pain as knee joint pain has been reported in children with HMS (Kerr et al. 2000; Vougiouka et al. 2000). Reduced knee flexion reported by Engelbert et al. (2004) may actually indicate the presence of knee pain in the children with HMS.

At the moment, there are only three studies that have been found (Engelbert et al. 2003; 2004; 2006) by the present author that have investigated ROM in children with HMS. Sample size and different experimental protocols limit the generalisability of these studies to other children with HMS. Therefore, a cross-sectional study with a larger sample size is required to identify the extent of knee ROM in children with HMS and their healthy counterparts.

#### **2.5.2.5 Other Musculoskeletal Features**

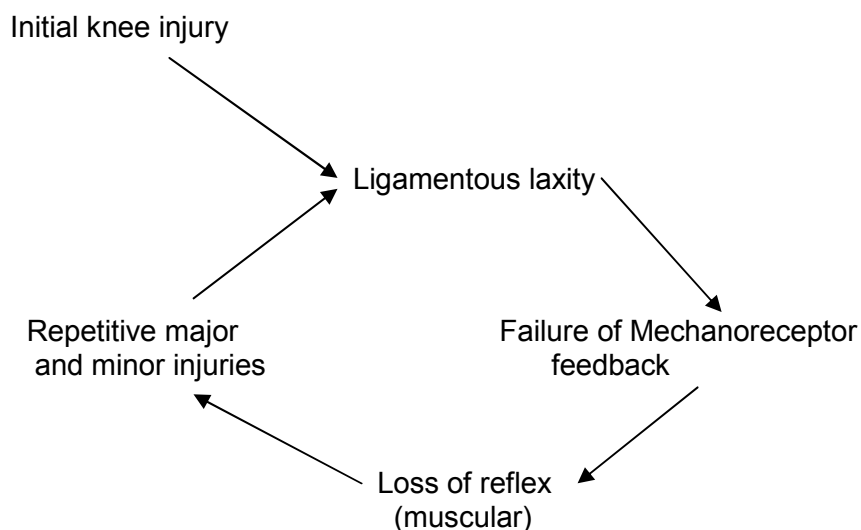
There are many other musculoskeletal problems that may be found in patients with HMS, although their occurrence may not be as frequent as those previously discussed (section 2.4.2.1 to 2.4.2.4). Grahame et al. (1981) reported that spinal X-rays of HMS patients revealed that 14 (58.3%) out of 24 compared with 3 (23%) out of 13 controls had spinal abnormalities such as scoliosis, transitional vertebrae at the lumbosacral junction, and pars interarticularis defects with or without spondylolisthesis. Similarly, Bridges et al. (1992) observed that 35% of HMS patients had a scoliosis.

A strong correlation between craniomandibular disorder (CMD) and GJL was observed by Westling (1989) when 74 patients (mean age 23.9 years) with CMD and 73 controls (mean age 24.8 years) were investigated. The prevalence of symptoms and signs of internal derangement in the temporomandibular joint (TMJ) were found to be higher in adolescents with GJL (Westling and Mattiasson 1992). These researchers examined 96 girls and 97 boys (all aged 17 years) for TMJ derangement and associated GJL. The findings of Westling (1989) and Westling and Mattiasson (1992) suggest that individuals with GJL may be seen with CMD and TMJ disorders.

Francis et al. (1987) demonstrated an association between HMS and peripheral neuropathy. All 11 HMS patients studied were found with tarsal tunnel syndrome (nerve disease due to compression of the posterior tibial nerve in the ankle and foot). Similarly, carpal tunnel syndrome (nerve disease due to compression of the median nerve) and sciatica have been demonstrated in patients with HMS (March et al. 1988; Beighton et al. 1989).

It is believed that lax joints are likely to be less stable and are generally more susceptible to subluxation or dislocation (Grahame 1981). Individuals with HMS may be predisposed to musculoligamentous lesions (Bulbena et al. 1992; Diaz et al. 1993). An association between GJL and musculoligamentous lesions has been demonstrated (Diaz et al. 1993). A higher frequency of joint dislocation, shoulder capsulitis and muscle tears in HMS subjects have been reported by Grahame et al. (1981). Additionally, Grahame et al. (1981) found a history of previous fracture in 52% of HMS patients compared with only 15% in the controls ( $p<0.05$ ). They also found a significant increase in the incidence of ligament injuries in patients with HMS compared with the controls ( $p<0.05$ ).

Bulbena et al. (1992) investigated 114 HMS patients (mean age 41.8 years) and 59 controls (mean age 48.1 years) and found that 7.1% of the HMS patients were reported to have had luxations and subluxations. No subjects among the controls were found with any of these features. The possible association between ligamentous laxity and musculoskeletal lesion injury in individuals with HMS is shown in Figure 2.4.



**Figure 2.4: The knee injury cycle (Adapted from Barrack and Munn 2000): Reduced feedback from mechanoreceptors due to joint laxity may lead to joint injury.**

Muscle/ligament/tendon sprains or strains of the lower limbs have been reported to be the most common injuries sustained by ballet dancers with GJL (Klemp et al. 1984). They observed that 33.3% of ballet dancers with GJL and 25% of the controls had sustained injuries while dancing, although this difference was not statistically significant. On the other hand, when the actual number of injuries sustained by each group was compared, the difference was statistically significant ( $p < 0.05$ ). In another study of HMS patients by Mishra et al. (1996), 10% were found with a history of soft tissue lesions such as ligament injuries.

In summary, joint laxity may predispose to spinal instability and the development of scoliosis in individuals with HMS. It also seems that TMJ dysfunction may coexist with GJL in adolescents with HMS. In addition, peripheral nerve compression appears to be a feature of HMS and subluxation and ligamentous injuries may also be features. Because the present study focused on the most commonly reported musculoskeletal symptoms in children with HMS, future research on HMS may be directed towards investigating these less common musculoskeletal features.

The following section discusses gait abnormalities that may be found in individuals with HMS.

### **2.5.3 Gait Patterns**

It has been suggested that abnormal joint biomechanics may be a feature of HMS (Grahame 1990, Hall et al. 1995) and gait abnormalities have been reported in children with HMS (Adib et al. 2005). Children with HMS often present with abnormal pronation of the feet at the subtalar joints (a result of joint laxity), which can contribute to lower limb symptoms (Maillard and Murray 2003). It is thought that a combination of GJL, reduced joint proprioception, muscle weakness and reduced stamina may affect the gait of a child with HMS (Maillard and Murray 2003).

During an in-depth literature search by the author of this thesis, only two studies (Engelbert et al. 2004; Adib et al. 2005) were found that have investigated gait patterns in children with HMS. Due to the limited information, the possible reasons for gait abnormalities in addition to the evidence in children with HMS are discussed in this section.

Engelbert et al. (2004) investigated gait patterns in 19 children (boys and girls; mean age 11.6 years) with HMS and found that 14 (74%) with habitual toe-walking. Information regarding this was obtained using a parental questionnaire. Although the finding of Engelbert et al. (2004) provides useful preliminary information on possible gait abnormality in children with HMS, their results could have been compared with healthy children to determine group differences. In addition, information recorded by parents of the participating children with HMS may not be accurate. Adib et al. (2005) reported abnormal gait patterns of children with HMS (aged < 18 years). In that study data was collected both retrospectively and prospectively on children with HMS. The findings may not accurately reflect children with HMS as important details might not have been documented on children whose data was recorded retrospectively. Additionally, they failed to specify the abnormalities in children with HMS and how they were examined for these. Therefore, it is unknown whether there is abnormal knee joint movement during walking or not.

Ligamentous laxity is considered to be the most common aetiological factor for flexible flatfoot in children (Thomson and Volpe 1993). Troott (1982) believed that laxity in the calcaneonavicular or 'spring' ligament may result in flatfoot deformity. El-Garf et al. (1998) found that 35.4% of Egyptian children (mean age 11.1 years) with GJL were found with flat feet. In another study by Bridges et al. (1992), 130

consecutive patients (age 18 years and over) referred to a rheumatology clinic were evaluated for musculoskeletal problems. It was discovered that 85% of 20 patients diagnosed with HMS had flat feet.

An abnormal propulsive pronation with marked Helbig's sign (bowing of the tendo Achilles) was observed in a 29-year old male patient with HMS by Grahame (2003). In addition, Grahame (2003) stated that during gait the foot of an individual with HMS may function around an abnormally pronated position, or may move in the direction of pronation at the time it should be supinating. It has been suggested that pronation of the foot may influence the kinematic pattern of the lower limb, particularly at the knee joint as the tibia internally rotates when the foot pronates during early stance (Perry 1992). Rotation of the tibia is in response to the medial rotation of the talus as it falls into the space created by the inferior and lateral movement of the calcaneus (Perry 1983). Therefore, from a clinical perspective, it can be assumed that increased foot pronation results in excessive internal rotation of the tibia and femur, which, in turn, increases the rotatory stresses at the hip and the knee joints (Tiberio 1987).

Since flat feet may be a feature of HMS, it seems likely that there may be abnormal foot pronation during walking in children with this condition. In addition, it appears that foot deformity (pes planus) may lead to abnormal gait biomechanics of lower limb joints (including the knee) in children with HMS.

The function of the quadriceps is to support and extend a flexed knee during walking (Perry 1992). It has also been suggested that rapid motion of the knee joint with intrinsic joint pathology may be limited such as articular surface damage, increases tissue tension and pain (Perry 1992). Knee joint pain may lead to limited knee flexion during the gait cycle (loading response, pre-swing and initial swing) as knee flexion is avoided during walking to escape the shear force that accompanies joint motion and to reduce the compressive force from a contracting quadriceps (Perry 1992). This may prevent the knee from being moved rapidly during walking and may result in inadequate arc of flexion during walking.

Putting the above observations (Engelbert et al. 2004; Adib et al. 2005) and assumptions together, it can be speculated that there may be abnormal joint kinematics during walking in children with HMS. Therefore, the gait kinematics of children diagnosed with HMS was therefore examined in this study to identify any deviation from normality.

The next section examines issues relating to quality of life (QoL) in children with HMS.

#### **2.5.4 Quality of Life (QoL)**

Quality of life (QoL) is the perception of a person's position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns (WHO 1995). The definition and measurement of QoL has been a subject of debate (Eiser and Morse 2001). According to these authors, there are many ideas that have defined the concept of QoL. First, it believed that individuals have their own unique perspective on QoL, which depends on present lifestyle, past experience, hopes for the future, dreams and ambition. Secondly, when QoL is used in medical context it is generally conceptualised as a multidimensional construct consisting of several domains. Thirdly, QoL can include both objective and subjective perspectives in each domain. Objective assessment of QoL focuses on what the individual can do, and is important in defining the degree of health. The subjective assessment of QoL includes the meaning to the individual and it involves the translation or appraisal of the more objective measurement of health status into experience of QoL. In patients there may be differences in appraisal which could account for the fact that individuals with the same objective health status can report very different subjective QoL.

Studies have shown that physical, psychological and social functioning may be affected in children with rheumatic conditions (Bailldam et al. 1995; Sawyer et al. 2004; Selvaag et al. 2003; Muller-Godeffroy et al. 2005) characterised by pain. The use of QoL as a treatment outcome measure in children with rheumatic diseases has been increasingly recognised (Epps et al. 2005; Powell et al. 2005). It has been suggested that activities of daily living and physical and sporting activities may be limited in children with HMS due to pain (Gurley-Green 2001; Murray and Woo 2001). No studies were found by the author of this thesis investigating QoL in



children with HMS. Therefore, it is unknown whether QoL is also affected in children with HMS compared with their healthy counterparts.

Since no data on QoL was found in children with HMS, studies that have investigated issues relating to physical, psychological and social functioning, believed to be components of QoL (Jette 1993) are examined in this section. It should however be noted that some of the studies (Arroyo et al. 1988; Mikkelsen et al. 1996; Adib et al. 2005) reviewed in this section were also discussed earlier in this chapter (section 2.3.2 and 2.4.1).

It has been suggested that the onset of musculoskeletal symptoms of HMS in adolescents may be frightening and may cause them additional distress (Middleditch 2003). Grahame (2000a) also believed that anxiety and depression are commonly expressed by patients with HMS. Moreover, individuals with HMS may avoid movement or activity that becomes painful (Middleditch 2003). Anxiety and panic disorders in individuals with HMS has been attributed to pain, instability and frequent injury (Russek 1999) which may be the result of ligamentous laxity and muscle imbalance. Furthermore, children with HMS may be labelled as being inattentive in their classroom (Middleditch 2003).

No difference in the rate of school absence was found in 66 healthy school children with GJL and 20 children with HMS by Arroyo et al. (1988). In another study, Mikkelsen et al. (1996) examined the level of physical activity participation and disability in healthy school children with GJL and controls. The children's participation level was examined with a questionnaire containing the following alternatives: I exercise to breathlessness at least half an hour (1) one to two times a week, (2) three to four times a week, (3) five to six times a week, (4) I do not exercise. Disability was determined subjectively using the following alternatives: (1) I have difficulty falling asleep because of aches and pains; (2) because of pain, I have difficulties in sitting during lesson; (3) pain disturbs me if I walk more than 1 km; (4) pain disturbs me during physical exercise class; (5) aches and pains disturb my hobbies. The disability index (maximum of 5) was calculated from these five types of disability.

No significant differences (p values not reported) were found in the level of physical activity participation and disability indices between the two groups. The protocol of Mikkelsen et al. (1996) was not described in detail and the instruction on how children completed the questionnaire regarding their physical activity and disability was not clearly stated. In addition, no information was given regarding how the items on the questionnaire were scored. Although a good test-retest repeatability ( $\kappa = 0.9$ ) of their questionnaire was reported, no information was given about its predictive validity. All the above factors could have contributed to the findings.

Higher prevalence of anxiety disorders have been found in rheumatological patients with GJL (Bulbena et al. 1993). Martin-Santos et al. (1998) also observed an association between GJL and patients diagnosed with anxiety disorders (panic disorder and or agoraphobia). They found that 67.7% of 99 patients with anxiety disorders had GJL using Beighton score  $\geq 5$ . Bulbena et al. (2004) reported a weak but significant association ( $r$  range = 0.10 to 0.16;  $p$  range = 0.0002 to 0.01) between GJL and anxiety disorders in individuals receiving medical check-ups. The latest three studies (Bulbena et al. 1993; Martin-Santos et al. 1998; Bulbena et al. 2004) were conducted in adults with GJL and associated anxiety disorders, therefore their findings may not be applicable to children with HMS.

Functional ability and physical and psychosocial well-being of school children with GJL and children without GJL was investigated by Ruperto et al. (2004) using the child health assessment questionnaire (CHAQ) and child health questionnaire (CHQ). These questionnaires were completed by the parents of the participating children. They observed that children with GJL were rated similar to their healthy counterparts by their parents except for a borderline limitation in role/social subscale ( $p = 0.04$ ) of the CHQ. Their findings might have been influenced by the following factors: (1). it is possible that the children's health status was under-rated by their parents as it has been found that parents of children with rheumatology conditions rated their children's QoL lower than the children themselves (Gong et al. 2007); (2). the questionnaires they used for evaluating health status in their study did not include any question on the ability of these children to perform demanding physical activities such as sports (Grahame 2000a) that are likely to affect the symptoms of HMS in children; (3). they investigated school children with GJL and not those with HMS. Therefore, their findings cannot be extended to those with HMS.

A range of functional difficulties have been reported in children with HMS by Adib et al. (2005). They investigated 125 children aged <18 years with this condition and found that 66% reported problems with dressing, 69% with hand writing, 53% with reading, 49% with spelling and 41% with making and keeping friends. Their findings suggest that children with HMS may suffer from functional, school and social problems, however, due to a lack of parallel control group, it is difficult to draw a definite conclusion from that study. In addition, the data of some of the children was collected retrospectively therefore, the process of data collection might not have been standardised in their study.

To date, no study has examined all the different components of QoL in children with HMS. Given that numerous separate observations and assertions have linked GJL to anxiety disorders and that poorer QoL has been reported in children with rheumatological conditions (Bildam et al. 1995; Sawyer et al. 2004) compared with healthy children, it is possible that QoL may also be affected in children with HMS. Hence, this provided strong justification for QoL assessment in children diagnosed with HMS.

## **2.6 Overall Summary**

This chapter has discussed the prevalence of generalised joint laxity (GJL) and HMS in children. It has also examined the aetiology and clinical features of HMS. The prevalence of GJL has also been reported to be as high as 64.9% in preschool children (Lamari et al. 2005) and HMS was observed in 26% of paediatric rheumatological referrals (Kerr et al. 2000). The prevalence of arthralgia was found in 55% of healthy school children with GJL and was reported in 74% of children with HMS (Adib et al. 2005). The knee joint has been reported to be the most commonly affected joint with the symptoms of HMS (Lewkonia and Ansell 1980; Finsterbush and Pogrund 1982; Kerr et al. 2000; Vougiouka et al. 2000; Adib et al. 2005). From the review of literature in this chapter it is clear that children with HMS may present with a range of neuromuscular impairments such as pain, muscle weakness and impaired joint proprioception. In addition, they may also be found with activity limitations such as abnormal gait patterns and participation restrictions in terms of functional difficulties, school problems, and social difficulties.

At present, the range of neuromuscular impairments, activity limitations and participation restrictions has not been well documented in children with HMS. The available published literature has been reported mainly in adult populations and may not be transferable to paediatric populations with this condition. Because of these reasons, it is difficult to conclude whether these variables are affected in children with HMS. To date, the relationships between the symptoms of HMS and their implications for function and QoL are unknown. Therefore, this study was designed to identify the level of neuromusculoskeletal impairments, functional ROM during walking and QoL associated with HMS in children.

The next chapter review the methods of assessing GJL, HMS, musculoskeletal impairments, functional ROM during walking and QoL in children.

## **CHAPTER 3 : DIAGNOSTIC CRITERIA FOR GENERALISED JOINT LAXITY AND HYPERMOBILITY SYNDROME IN CHILDREN, AND METHODS OF ASSESSING THE ASSOCIATED FACTORS**

### **3.1 Introduction**

In the previous chapter, the possible neuromusculoskeletal impairments, gait patterns and level of quality of life (QoL) associated with HMS were discussed. There are many diagnostic criteria developed for defining generalised joint laxity (GJL) and hypermobility syndrome (HMS). These methods include the Carter and Wilkinson scoring system (1964), Beighton et al. (1973), Bulbena et al. (1992) and Brighton criteria (Grahame 2000a). There are currently no agreed criteria for assessing GJL and HMS although, a set of diagnostic manoeuvres proposed by Carter and Wilkinson (1964), modified by Beighton et al. (1973) are often used. Unfortunately, these methods are insensitive, subjective and not standardised.

Beside these tools, other instrumental methods have been used to assess joint laxity associated with HMS. These include the hyperextensometer (Bird et al. 1979), fixed torque device (Jobbins et al. 1979), and universal goniometers (Mishra et al. 1996). Although such instruments are quantitative means of clinical assessment they may not be sensitive to clinical changes and only assess joint laxity (one of the key features associated with HMS) without its associated symptoms. Therefore, their clinical utility for diagnosing children with HMS is limited. The inability of such methods to detect the various clinical features of HMS might have contributed to the concern that some researchers and clinicians have regarding clinical assessment of children with HMS. For example, Cherpel and Marks et al. (1999) and Ferrell et al. (2004) believed that patients with HMS may be missed out during clinical assessment and may not receive the appropriate treatment for their condition.

The traditional diagnostic tools used for HMS do not include assessment of the key features that may be associated with this condition such as musculoskeletal impairments (range of motion (ROM), pain, proprioception and muscle strength), functional ROM during walking and QoL. There are many methods of assessing these key factors in children. Some of these methods may be time consuming, expensive and pose some ethical issues. This chapter examines the strengths and weaknesses of various methods of assessing GJL and HMS. It also discusses

issues related to assessment of neuromuscular impairments, functional ROM during walking and QoL in children. Moreover, methods of gait analysis and QoL assessment are examined. The methods of assessing joint proprioception are discussed in chapter four of this thesis.

### **3.2 Diagnostic Criteria for Generalised Joint Laxity and HMS**

There are many diagnostic criteria developed for assessing generalised joint laxity (GJL) and HMS (Cherpel and Marks 1999; Van der Giessen et al. 2001). The most widely used are the Beighton criteria, which are believed to be easy and suitable for epidemiological studies (Larsson et al. 1993). The range of diagnostic criteria are described below.

#### **3.2.1 The Carter and Wilkinson Diagnostic Criteria**

The first scoring system for assessing GJL was developed by Carter and Wilkinson (1964). The scoring scale or rating is a qualitative assessment of the ability to perform the following movements: 1) passive apposition of the thumb to the flexor aspect of the forearms; 2) passive hyperextension of the finger to  $\geq 90^{\circ}$ ; 3) passive elbow hyperextension beyond  $10^{\circ}$ ; 4) passive knee hyperextension beyond  $10^{\circ}$ ; 5) excessive passive ankle dorsiflexion and eversion. Using this set of criteria, one point is usually assigned to each lax joint. GJL is diagnosed in the presence of  $\geq 3$  scores out of 5, while a child is said to have HMS with a score of  $\geq 3$  in the presence of musculoskeletal pain.

The validity of Carter and Wilkinson's method was examined by Bulbena et al. (1992) in healthy adults and those with HMS. They found a high Spearman's rho correlation coefficients ( $r = 0.91$ ) between the Carter and Wilkinson and Beighton criteria suggesting that there was a high concurrent and predictive validity between the diagnostic criteria. A good interater repeatability (Kappa coefficients  $>0.7$ ) of the Carter and Wilkinson criteria was also demonstrated by Bulbena et al. (1992). These criteria are time efficient and easy to administer.

However, the Carter and Wilkinson method is subjective, non standardised and limited in scope. It only takes into consideration joint ROM and pain in HMS patients rather than the other symptoms such as muscle weakness, proprioception and QoL. These criteria take into consideration certain specified joints, thereby missing out some other joints that might be symptomatic such as the shoulder joint. The sensitivity of this method has not been reported. Carter and Wilkinson criteria were designed for young children and they may not be appropriate for use in older children.

### **3.2.1 The Beighton Criteria**

Beighton criteria are modifications of the Carter and Wilkinson criteria by Beighton et al. (1973). They were developed for use in an epidemiological survey of bone and joint disorders (Bulbena et al. 1992; Grahame and Bird 2001) and were first used for assessing 300 healthy children and adults in a rural community in South Africa by Beighton et al. (1973). The Beighton criteria (Table 3.1 and Figure 3.1) consist of five scoring items. One point is assigned for each lax joint with one additional point for excessive forward trunk flexion.

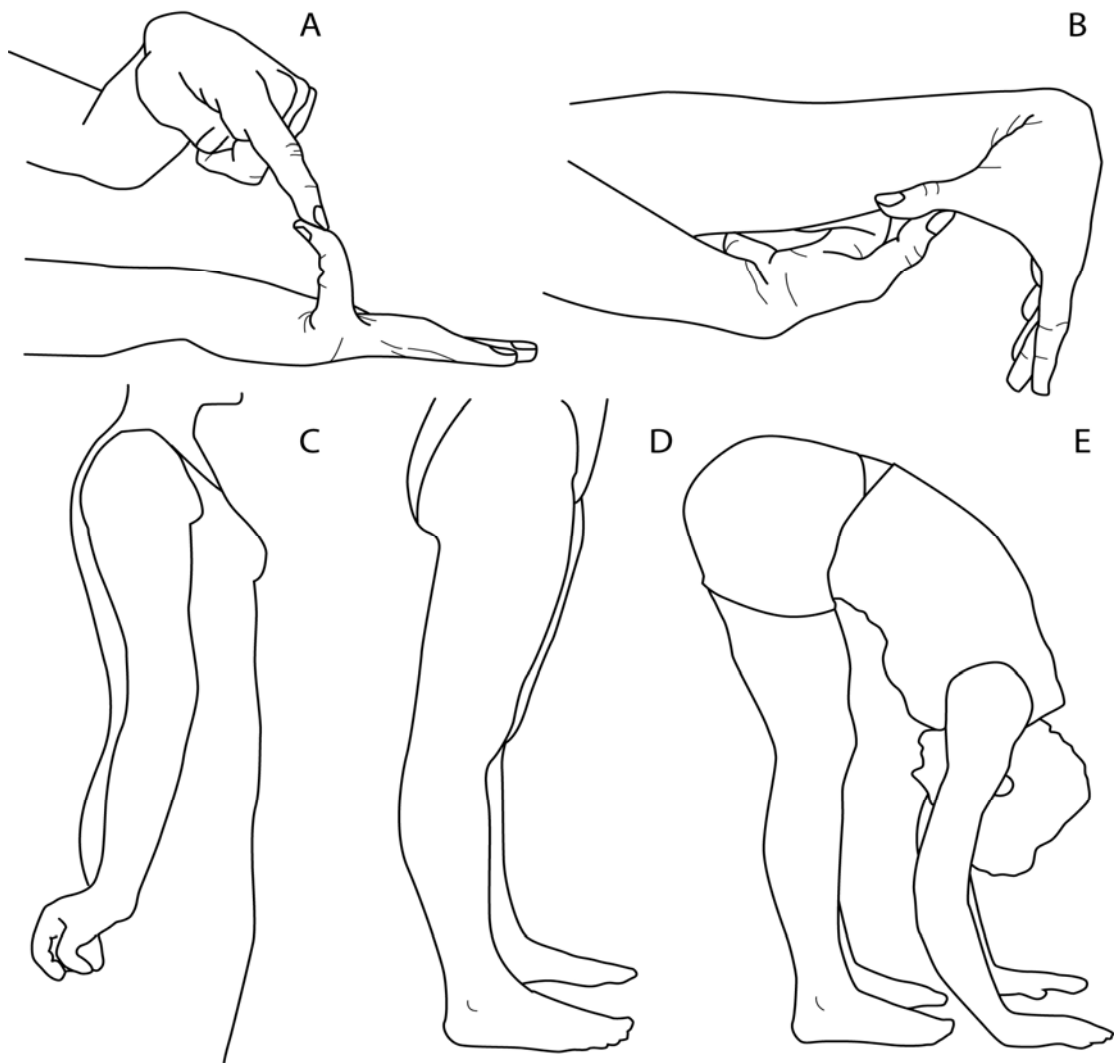
Beighton criteria constitute the most widely used assessment tool for large population studies concerning GJL and HMS. However, there is no universally accepted Beighton score for the diagnosis of GJL and HMS (Maillard and Murray 2003). A minimum score of 4/9 has been considered for diagnosing GJL and a score of 4/9 with associated musculoskeletal complaints such as pain has been used as the diagnostic cut-off point for HMS (Tables 2.1 and 2.2). The Beighton criteria are accurate, easy to use and are not time-consuming (Klemp et al. 1984), and have recently been validated in children (Van der Giessen et al. 2001). Additionally, excellent intra-rater repeatability (ICC = 0.84) and inter-rater repeatability (ICC = 0.80) of the Beighton criteria have been reported in healthy school children by Mikkelsen et al. (1996). In addition, the Beighton criteria have been reported to have low inter-rater variability by clinicians when used for assessing children (Hansen et al. 2002). The Beighton criteria have one advantage over the Carter and Wilkinson (1964) method in that they cover more joints. However, it is believed that the spinal flexion test is the least useful (Lewkonja 1987) as it is influenced by age, limb length, and even repetitive hamstring stretching (Klemp et al. 1984). Although the Beighton criteria give a widespread nature of joint laxity in individuals with HMS,

they give no indication of the degree of joint laxity (Grahame and Bird 2001) at specific joints. Moreover, the severity of symptoms of HMS in children is also not taken into consideration by Beighton criteria. Therefore, there is a risk that pauci-articular HMS may be missed during clinical assessment using this method.

**Table 3.1: The nine point Beighton criteria (Adapted from Grahame 1999; Van der Giessen et al. 2001): One point may be gained on each side (right or left) for activities A-D and a total score of 9 points can be achieved if all are positive.**

Activity	Right	Left
A) Passive dorsiflexion of the fifth metacarpophalangeal joint to 90° with the wrist in mid position.	1	1
B) Passive opposition of the thumb to the volar aspect of the ipsilateral forearm.	1	1
C) Hyperextension of the elbow greater than 10°.	1	1
D) Hyperextension of the knee more than 10°.	1	1
E) Bending forward to place hands flat on the floor without bending the knees.		1
Total possible score		9





**Figure 3.1: The Beighton criteria for generalised joint laxity (illustration by Steve Kelly, Manchester Metropolitan University)**

Beighton criteria overlook several joints that have a tendency to develop HMS-related symptoms, such as the shoulder and ankle. The criteria do not take into account the reduction in GJL with age, as GJL varies with age and health status (Cherpel and Marks 1999). Furthermore, these assessment criteria are a qualitative means of diagnosing HMS. The method only takes into consideration the joint ROM and pain in HMS patients rather than other key symptoms that may be associated with the condition.

### **3.2.2 Contompasis Assessment Method**

The Contompasis method (Table 3.2) proposed by McNerney (1979) is a further modification of the Beighton criteria (McCormack et al. 2004). It is believed that the Contompasis method gives a more refined grading by allowing between two and six (eight in case of the forward flexion test) points for each of the nine Beighton scores (Grahame 2003b). Contompasis introduces a sixth test (test of hindfoot eversion) with a range of between two and seven points. Excluding the hind foot eversion test, this scoring system has a total of between two and 56 points (Cherpel and Marks 1999). However, if the foot eversion test is included, the maximum range extends from two to 70 points (Grahame 2003b). It provides a means of measuring joint ROM through the normal range into the hypermobile end. The Contompasis method is a semi-quantitative measure of GJL (McCormack et al. 2004) and the most comprehensive of all the assessment criteria (Bird 2004). A strong and significant correlation ( $r = 0.87$ ;  $p = 0.001$ ) was observed between the Beighton and Contompasis methods (Ferrell et al. 2004). Although the use of Contompasis method for diagnosing GJL and HMS is becoming popular (Mishra et al. 1996; Ferrell et al. 2004; McCormack et al. 2004; Ferrell et al. 2007), it is complex and time consuming. Information on neuromusculoskeletal impairments and the level of QoL characteristics associated with HMS may not be necessary for diagnosing HMS, but would have been better if the method provided some information regarding other factors that may be associated with this condition. Therefore, there are limitations to its use for assessing children diagnosed with HMS.

**Table 3.2: The Comtopasis scoring scale (Adapted with permission from Cherpel and Marks 1999)**

Manoeuvre description	Scoring criteria
1. Passive apposition thumb to flexor aspect forearm ("thumb to wrist test"). Points allocated according to the extent to which thumb meets or passes forearm.	Thumb not touching flexor aspect of forearm and separated from it by 30° to 75°-2 points Thumb touches the forearm-4 points Thumb digs into the forearm easily-5 points Thumb can be pushed beyond axis of forearm-6 points
2. Passive extension fifth metacarpophalangeal joint. The angle measured is the long axis of the forearm with the long axis of the fifth digit.	Hyperextension between 30° and 85°-2 points Hyperextension of 90°-100°-4 points Hyperextension of 100°-120°-5 points Hyperextension > 120°-6 points
3. Passive hyperextension of the elbow. The angle measured is the long axis of the forearm with the long axis of the upper arm.	Hyperextension between 0° and 5°-2 points Hyperextension between 10° and 15°-4 points Hyperextension between 16° and 20°-5 points Hyperextension > 20°-6 points
4. Passive hyperextension of the knee.	Hyperextension of 0°-5°-2 points Hyperextension of 10°-15°-4 points Hyperextension of 16°-20°-5 points Hyperextension > 20°-6 points
5. Forward flexion of the spine, attempting to place the hands flat on floor in front of feet (which are together) without bending the knees.	No contact with ground-2 points Fingertips touch ground-4 points Fingers touch ground-5 points Palms can be placed flat on ground-6 points Wrists can be placed on ground-7 points Forearm reaches ground-8 points
6. Foot flexibility test (ankle extension and calcaneal stance position). The degree of eversion of the calcaneus is recorded.	0°-2° of eversion-2 points 3°-5° of eversion-4 points 6°-10° of eversion-5 points 11°-15° of eversion-6 points more than 15° of eversion-7 points

Movements 1-5 are replicated from the Beighton criteria but higher points are allocated to the degree of GJL scored (2-56 with foot test excluded; 2-70 with foot test included). Please note that movements 1-4 and 6 are scored bilaterally.

### **3.2.3 Bulbena Criteria**

The presence of GJL can also be measured using the Bulbena score (Bulbena et al. 1992; Engelbert et al. 2005). These are a set of 10-point Hospital del Mar (Barcelona) criteria (Bulbena et al. 1992). The Bulbena criteria (Table 3.3) are an alternative scoring system for GJL and HMS, introduced to obtain detailed information about ecchymoses and the presence of GJL in nine joints (little finger, thumb, elbow, shoulder, hip, knee, patella, ankle and first metatarsophalangeal) overlooked by the Beighton criteria (Bulbena et al. 1992).

An advantage of this scale is that some other parts of the body that can easily yield useful evidence of the symptoms of HMS have been incorporated. On the other hand, this scale is a subjective form of diagnosis of HMS. Consequently, there are limitations to its use in children with HMS.

The Bulbena score is made up of gender-related cut-off points. In girls, a score of greater than 5 and in boys 4 are used to determine the presence of GJL. The Bulbena scoring system has been found to have high concurrent validity with the Beighton score and high test-retest repeatability in adults (Bulbena et al. 1992). The test-retest repeatability of the Bulbena scoring system has also been reported to be excellent in children (Engelbert et al. 2005).

**Table 3.3: Bulbena Criteria (Adapted from Cherpel and Marks 1999; Bulbena et al. 2004): In girls, GJL is diagnosed by the presence of a score greater than 5 and a score greater than 4 in boys indicate the presence of GJL.**

#### **Upper Limb**

Thumb: Passive apposition of the thumb to the flexor aspect of the forearm at  $<21\text{mm}$ .

Metacarpophalangeal: With the palm of the hand resting on the table, the passive dorsiflexion of the fifth finger is  $>90^{\circ}$ .

Hyperextension of the elbow: The passive extension of the elbow is  $\geq 10^{\circ}$ .

External rotation of the shoulder: With the upper arm touching the body and with the elbow flexed at  $90^{\circ}$ , the forearm is taken in external rotation  $\geq 85^{\circ}$  of the sagittal plane (shoulder to shoulder line).

#### **Lower Limb, Supine Position**

Hip abduction: The passive hip abduction can be taken to an angle of  $\geq 85^{\circ}$ .

Patellar hypermobility: With one hand holding the proximal end of the tibia, the patella can be moved well to the sides with the other hand.

Ankle and feet hypermobility: An excess range of passive dorsiflexion of the ankle and eversion of the foot can be produced.

Metatarsophalangeal: Dorsal flexion of the toe foot over the diaphysis of the first metatarsal is  $\geq 90^{\circ}$ .

#### **Lower Limb, Prone Position**

Hyperextension of the knee: Knee flexion allows the heel to make contact with the buttock.

#### **Ecchymoses**

Ecchymoses: Appearance of ecchymoses after hardly noticed, minimal traumatism.

### 3.2.4 Brighton Assessment Criteria

Because there is an overlap between HMS and heritable disorders of connective tissue, the Brighton criteria (Table 3.4) have been developed (Grahame 2000a). They were proposed by the British Society for Rheumatology in 1992 (Mikkelsen 1996). These diagnostic criteria are a combination of Beighton criteria and definitions of the duration of symptoms and range of arthralgia (joint pain) (Bird 1992). They include several clinical features as well as range of joint movement. They are used for classifying HMS and not GJL (Maillard and Murray 2003). The Brighton criteria consist of major criteria and minor criteria (Table 3.4).

**Table 3.4: The Revised Brighton Criteria for HMS (Adapted from Grahame 2000a): HMS is diagnosed by the presence of the two major criteria, or one major and two minor criteria, or four minor criteria.**

#### **Major criteria**

1. A Beighton score of 4/9 or more (currently or historically)
2. Arthralgia for longer than 3 months in 4 or more joints

#### **Minor criteria**

1. A Beighton score of 1, 2 or 3/9 (0, 1, 2, or 3 if aged 50 years plus)
2. Arthralgia ( $\geq 3$  months) in 1–3 joints, or back pain ( $\geq 3$  months), spondylosis, spondylolysis/spondylolisthesis
3. Dislocation/subluxation in more than one joint, or in one joint on more than one occasion
4. Soft tissue rheumatism  $\geq 3$  lesions (e.g. epicondylitis, tenosynovitis, bursitis)
5. Marfanoid habitus: tall, slim, span:height ratio  $>1.03$ , upper:lower segment ratio  $<0.89$ , arachnodactyly (+ Steinberg/wrist signs)
6. Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring
7. Eye signs: drooping eyelids or myopia or antimongoloid slant
8. Varicose veins or hernia or uterine/rectal prolapse

It is believed that two minor criteria will suffice where there is an unequivocally affected first-degree relative (Grahame 2000a). However, HMS is excluded by the presence of Marfan or Ehlers-Danlos syndromes (EDS) (other than the EDS hypermobility (GJL) type). Moreover, major criteria 1 and minor 1 are mutually exclusive and major 2 and minor 2 (Grahame 2000a).

The advantage of these criteria over the others is that they take into consideration associated symptoms (such as joint pain and dislocation/subluxations) and their duration in relation to HMS. However, Brighton criteria are a qualitative means of diagnosis. The validity, repeatability and sensitivity of the Brighton criteria have not been reported in children. Therefore, there are limitations to the use of the Brighton criteria in clinical assessment of HMS in children.

In summary, there are various diagnostic methods for GJL and HMS. These scoring systems are believed to provide an approximate quick guide on GJL and HMS (Bird 2005). However, they are subjective and hence are prone to bias. In addition, they do not accurately quantify the extent of joint laxity and pain for other purposes. Although these diagnostic tools were designed to incorporate the ROM and pain associated with HMS, they would have been more appropriate for clinical assessment if other important symptoms such as muscle weakness (Middleditch 2003; Sahin et al. 2007), impaired joint proprioception (Mallik et al. 1994; Hall et al. 1995) and functional difficulties (Adib et al. 2005) associated with HMS were included in the tools. Furthermore, there are no agreed criteria and cut-off point for diagnosing GJL and HMS.

### **3.3 Measuring Devices for Joint Range of Motion (ROM)**

The previous section demonstrated that the existing diagnostic criteria used for assessing GJL are subjective and only consider the widespread nature of joint laxity and pain associated with GJL. They do not give enough indication of the extent of joint laxity and when GJL become symptomatic. This implies that these methods of diagnosis may not be sensitive to detecting clinical changes in children with HMS.

GJL is a necessary feature of HMS in children (Arroyo et al. 1988) and has been measured subjectively using the criteria described in section 3.2. Only two studies have examined GJL in children with HMS using an objective measure (Engelbert et al. 2003; 2006). If clinical changes associated with HMS are to be monitored effectively, it is important to measure ROM objectively. Therefore, relevant methods of assessing ROM in children are examined in this section.

#### **3.3.1 Range of Motion (ROM)**

Joint range of motion (ROM) can be examined by performing various active and passive joint motions. Joint motion is a necessary component of most functional tasks (Clarkson 2000). It is believed that careful examination of joint range of motion, end-feel, effect on symptoms, and pattern of limitation help to identify and quantify impairments causing functional disabilities, and to determine the structures that require treatment (O'Sullivan and Schmitz 2001). Joint ROM can be affected by pathology, muscle strength, oedema, age, activities, gender, joint enlargement, and joint deformity (Norkin and White 2003).

##### **3.3.1.1 Types of Movements**

Essentially two types of motion can be achieved in a joint; the passive ROM (PROM) and the active ROM (AROM). Passive motions are movements performed by the examiner without the assistance of the patient (Maitland 1991; Clarkson 2001; Petty and Moore 2001). Normally, PROM is slightly greater than the AROM because joints have a small amount of motion at the end of the range that is not under voluntary control (Clarkson 2001; Petty and Moore 2001). This additional range helps to protect joint structures by allowing the joint to absorb extrinsic forces. PROM is examined not only for amount of motion, but also for motion's effect on symptoms, end-feel, and pattern of limitation (Norkin and White 2003).



PROM depends on the integrity of the joint surfaces and the extensibility of the joint capsule, ligaments, muscles, tendons and soft tissue. Limitations in PROM may be due to bony or joint abnormalities or tightness of the associated soft tissues (Clarkson 2001; Petty and Moore 2001; Norkin and White 2003). Because the examiner provides the force needed to perform PROM, rather than the patient, PROM does not depend on the patient's muscle strength and coordination. The AROM is the unassisted voluntary movement of a joint (Petty and Moore 2001; Trew and Everett 2001). Different methods of assessing ROM are discussed below.

### **3.3.2 Fixed Torque Device (FTD)**

This measuring device was developed by Silman et al. (1986). The device was first used and validated for index finger hyperextension by Jobbins et al. (1979) and was modified by Silman et al. (1986) to measure the index finger hyperextension, forearm rotation (total range – pronation plus supination), and lower limb rotation (total range – external plus internal rotation).

This method was used to assess the distribution of mobility in a normal adolescent population (Silman et al. 1986). A fixed torque device (FTD) is easy to use and provides the examiner with quantitative data. However, the device is expensive and not readily available for clinical use. Therefore, it was not used in the present study for assessing ROM.

### **3.3.2 Gravity-Dependent Goniometer**

Gravity-dependent goniometers or inclinometers use gravity's effect on measured fluid levels to measure ROM (Clarkson 2001; Norkin and White 2003). There are various types of gravity-dependent goniometers such as pendulum, fluid (bubble), Myrin goniometer (LIC, Sweden) and cervical range of motion (CROM) (Lea and Gerhardt 1995). These goniometers use a pendulum needle that reacts to gravity to measure motions in frontal and sagittal planes and uses a compass needle that reacts to the earth's magnetic field to measure motion in horizontal plane.

They are usually attached to the distal segment of the joint being measured. They may be easy to use for certain joints (spinal joints) because they do not have to be aligned with bony landmarks or centred over the axis of motion (Norkin and White 2003). However, to obtain accurate measurements it is important that the distal segment of the joint being measured be positioned vertically or horizontally. A good

test retest repeatability of gravity-dependent goniometers has been reported in healthy adults (Rheault et al. 1988; Bartholomy et al. 2000).

Rheault et al. (1988) investigated interrater repeatability and concurrent validity of a gravity-dependent goniometer for measuring active knee flexion in 20 healthy adults (mean age 24.8 years) in prone lying. Measurements with the goniometer were compared with those taken with a universal goniometer. A good interrater repeatability ( $r = 0.87$ ) was recorded for the two goniometers. The study by Rheault et al. (1988) was conducted on adults and their findings may therefore not be applicable to children. They also examined active knee ROM, rather than passive knee flexion to be assessed in this work. Gravity-dependent goniometers are difficult to use on small joints (Clarkson 2000) and where there is soft tissue deformity or oedema. Furthermore, they are also impractical for measuring knee flexion in supine, due to associated hip movement. Additionally, they are generally expensive. In view of these drawbacks, the gravity dependent goniometer was not used for assessing knee joint ROM in this study.

### **3.3.3 Visual Estimation**

Visual estimation is often used in clinical practice to assess ROM of patients, especially those with excessive soft tissue covering physical landmarks (Watkins et al. 1991). PROM of the knee joint in 43 adults (mean age 39.5 years) was examined using a universal goniometer and visual estimates by Watkins et al. (1991). The visual estimation method was reported to be less accurate and repeatable than the universal goniometers (Watkins et al. 1991) for measuring both knee flexion and extension. Visual estimation depends on the experience and judgement of the examiner. Additionally, it gives subjective information and may not be sensitive enough for clinical use. As a result of these limitations, visual estimation was not used for assessing ROM in this study.

### **3.3.4 Photography and Video Recording Equipment**

Photography has been used to measure joint ROM. Fish and Wingate (1985) reported that photography methods are more accurate than universal goniometry for measuring elbow joint ROM. Photography methods are more expensive and time consuming than other clinical methods. Video recording techniques have also previously been used to assess joint ROM (Norkin and White 2003). These techniques require the attachment of reflective markers on bony landmarks. An example is in motion analysis systems. These techniques depend on the examiners' experience in marker placement procedure. Skin movement may be associated with these techniques and may lead to measurement error. Video methods are generally expensive and require very large amount of space. Hence, video methods may not easily be available for clinical use. Hence, it was not used in the present study for measuring passive ROM of the knee joint.

### **3.3.5 Radiographic Technique**

This method is believed to be the '*gold standard*' against which all other techniques of joint ROM measurement are compared (Norkin and White 2003). Radiographic techniques have been used to measure the amount and type of motion occurring at the human knee joint (Enwemeka 1986). In a study of 10 healthy adults (age range = 21 to 35 years) by Enwemeka (1986) measurements of six knee joint angles (0, 15, 30, 45, 60, and 90 degrees) were compared using a universal goniometer and bone angle measurements provided by radiographs. A mean difference of 0.52 to 4.59 degrees (range) was reported, suggesting a low systematic difference between these methods of assessing ROM.

Although the study reported by Enwemeka (1986) examined the knee joints it had a small sample size. Additionally, it was conducted on healthy adults. Therefore, the findings from that investigation may not be applicable to children and subjects with pathological conditions. Moreover, routine and repeated exposure to radiation when measuring joint ROM using radiographic techniques may constitute health risks. This technique is expensive, may be time consuming and poses ethical issues. Therefore, its use in the clinical setting for ROM assessment in children is not desirable.

### **3.3.7 Electrogoniometers**

Electrogoniometers have been used in research studies to obtain dynamic joint measurements. The electrogoniometer is a strain gauge that converts angular motion of the joint into electrical signals (Reese and Bandy 2002). Many electrogoniometers are capable of measuring motion in several planes simultaneously. The test-retest repeatability of an electrogoniometer (Penny and Giles Ltd, Blackwood) for measuring the ROM of the first metatarsophalangeal joint in 14 healthy adults (mean age = 34 years) was reported by Bevens (1993) to be excellent (Pearson's Product Moment (PPM) Correlation = 0.90). The statistical analysis used (PPM) by Bevens et al. (1993) for assessing repeatability might not have been appropriate. PPM examines a relationship between two variables and not agreement between measurements (Bland and Altman 1996a; Rankin and Stokes 1998). Therefore, a good relationship between measurements obtained from the electrogoniometer used might not have been an indication of good agreement between its measurements.

Furthermore, the application of electrogoniometers requires examiner's skill as they are very difficult to align with the joint being measured. The use of electrogoniometers may be time consuming as they take time to calibrate accurately; they are also very expensive. Due to these disadvantages, they may not be suitable for assessing ROM in children diagnosed with HMS in a clinical setting. Hence, they were not used in the present study.

### **3.3.8 Universal Goniometer**

The universal goniometer is the instrument most commonly used to measure joint ROM in the clinical setting (Nokin and White 2003). It can be used to measure ROM in virtually all joints of the body (Nokin and White 2003). The universal goniometer may be made of metal or plastic and varies in shape and size. It consists of a protractor (metal or plastic) measuring  $0^{\circ}$  to  $180^{\circ}$  and from  $180^{\circ}$  to  $0^{\circ}$ , or from  $0^{\circ}$  to  $360^{\circ}$  and from  $360^{\circ}$  to  $0^{\circ}$ . The universal goniometer is made up of two arms (stationary and moving arm) and the overall length of each arm depends on the design of the goniometer. The two arms are secured through the centre of the protractor by a rivet or friction bolt. The measurement scales of the goniometer may vary from  $1^{\circ}$  to  $10^{\circ}$  increments.

Gogia et al. (1987) demonstrated an excellent criterion-related validity ( $r$  range = 0.97 to 0.98; ICC range 0.98 to 0.99) of passive knee flexion in 30 healthy volunteers aged 20 to 60 years using a universal goniometer. These authors also reported an excellent interrater repeatability ( $r$  = 0.98; ICC = 0.99) of passive knee flexion. The study by Gogia et al. (1987) has the advantage of having a good sample size. However, it was conducted in healthy adults and as a result the findings may not be transferable to children. Moreover, the details of their testing position were not given therefore it is possible that testing position was not standardised. Similarly, Pandya et al. (1985) reported a high test-retest repeatability (ICC range = 0.81 to 0.91) and low interrater repeatability (ICC range = 0.25 to 0.91) of passive knee extension measurements in children aged 1 to 20 years with Duchenne muscle dystrophy (DMD), using a universal goniometer. Universal goniometers are easy to use, inexpensive and are readily available for clinical use (Clarkson 2000).

In summary, review of the literature reveals that there are various methods of assessing ROM. Some of these methods have been reported to be valid means of evaluating ROM. Available evidence shows that some of these methods have been used mainly in healthy adults (Rheault et al. 1988; Bartholomy et al. 2000). The use of a technique like the radiographic method may pose ethical problems thereby limiting its routine use in assessing ROM in children.

Techniques like electrogoniometers, video recording and photography are expensive and time consuming. Moreover, an inexpensive method such as the visual estimate may not be sensitive enough for clinical use. Universal goniometers are easy to use, inexpensive and are readily available for clinical use (Clarkson 2000). Furthermore, their measures have been shown to be repeatable (test-retest repeatability) for assessing knee joint ROM in children with DMD. Consequently, the universal goniometer was used for assessing knee ROM in this study.

### **3.4 Clinical Methods of Assessing Pain**

The International Association for the Study of Pain (IASP 1994), defined pain as an unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage. Pain is a subjective feeling, with no known biological markers but a response to noxious stimuli. Pain may be modified by psychological factors such as state of mind, past experience and conditioning influences, as well as sociological factors such as gender and culture (French 1989).

Pain could be physical or psychological. Budd (1996) classified physical pain according to causes: 1. Nociceptive (stimulation of nociceptors). 2. Neurogenic (malfunction or damage to nervous tissues). 3. Sympathogenic (malfunction of the sympathetic arm of the autonomic system); and 4. Visceral pain (prolonged noxious stimulation of high threshold receptors, intensity-encoding receptors and silent receptors).

This section examines clinical methods of evaluating pain in children. Pain assessment is a critical component of pain management. There are a number of well-validated pain measuring instruments for children and adolescents (Walker et al. 1997; Streisand et al. 2001). Pain assessment in children is challenging since most of the methods used are subjective. However, objective evaluation of the nature and frequency of children's pain behaviours provides an accurate estimate of the strength of their pain experiences (McGrath and Brigham 1992).

There are several methods of measuring pain in children, such as physiological measures of pain (Hester 1993), visual analogue scale (McGrath 1987), parent post-operative pain measure (Chambers et al. 1996), adolescent paediatric pain tool (Savera et al. 1993) and faces pain scale (Chambers et al. 2003). Other types of self-report measures have also been developed for children such as the Poker chip tool (Romsing et al. 1996) and pain thermometer (Schanberg et al. 1997; Cheng et al. 2003). French (1989) believed that the presence of pain and measurement of its intensity rely entirely on the patient's self report.

As suggested by McGrath et al. (1996), a good paediatric pain measure must be valid, in that it clearly measures specific dimensions of a child's pain so that changes in ratings reflect meaningful differences in the child's experience. It must be repeatable regardless of the time of testing, age or gender of the child and regardless of who administers the measure to the child. Furthermore, the measure must be relatively free from response bias in that children use it similarly regardless of differences in how they wish to please adults or differences in how adults may administer it. Lastly, it must be versatile and practical for assessing different types of pain and for use in diverse clinical settings (McGrath et al. 1996). This following section examines in more detail some methods of assessing pain in children.

### **3.4.1 Adolescent Paediatric Pain Tool (APPT)**

The adolescent paediatric pain tool (APPT) is a multidimensional pain instrument for children and adolescents (Crandall and Savendra 2005). It consists of three components: 1) a body outline; 2) a 100-mm visual analogue scale with 5 equidistant pain intensity word anchors (i.e., a word-graphic scale); 3) a pain quality word descriptor list. Children are asked to rate their pain on the numeric rating scale, mark the areas on the body outline diagram (BOD) where he/she is having the worst pain or point to the words on the word descriptor list that best describes the pain when it was at its worst.

The validity and repeatability of each component of the APPT has been established in healthy and ill children (Savera et al. 1993). The adolescent paediatric pain tool provides children with a systematic method for describing the characteristic of their pain, intensity, and the body segments that are involved. This assessment tool has two limitations. First, it is time consuming. Secondly, where the child is not able to read the researcher is required to explain the procedure to the child. During the assessment procedure, the researcher might not interpret the response correctly. Due to the time involved in the administration of APPT, it was not used for pain assessment in this study.

### **3.4.2 Physiological Measures of Pain**

Physiological measures of pain have been used to indicate the presence of pain through changes in physiological variables assumed to be associated with pain (Hester 1993). Such variables include heart rate, vagal tone, respiratory rate and blood pressure. Others are palm sweating, oxygen saturation, transcutaneous oxygen tension, transcutaneous carbon dioxide and intracranial pressure (Hester 1993).

Physiological measures of pain give objective and quantifiable data. However, their validity and repeatability have been difficult to examine (Stevens et al. 1995). These measures require a large amount of staff training and expensive equipment. Also, many factors other than pain may affect physiological variables. Physiological pain measures cannot be used for retrospective pain assessment, for example pain in the last 2 days. Therefore, these pain assessment tools may not be sufficient to capture pain experienced by children with HMS. Thus, they were not suitable for use in this study.

### **3.4.3 Visual Analogue Scale (VAS)**

The visual analogue scale is a 10-cm line with the anchor words such as 'no pain' and 'the worst pain possible'. This scale is universally used. It is subject to bias but has proven to be repeatable and valid in children and adolescents of 9-15 years (McGrath 1987). Similarly, children aged 5 years and older have been able to use the VAS in a repeatable and valid manner to rate their pain intensity (McGrath et al. 1991). The scale requires children to mark a line at a point that matches the strength of their pain intensity.

Studies have shown that some VAS have ratio scale properties (McGrath et al. 1985) that can provide accurate estimates of pain intensity and percent changes in pain. Another type of VAS is the traditional VAS; with a black line drawn on a piece of paper (McGrath et al. 1996) and the clinician measures a child's response using a ruler. This may be time consuming for routine assessment of children's pain. Additionally, the measurement by the clinician using a ruler may not accurately reflect a child's response as it is prone to mistake on the part of the clinician. Moreover, a child's response may be influenced by numerical values on the scale. Because of this, VAS may not provide a true pain rating in children with HMS.



### 3.4.4 Coloured Analogue Scale (CAS)

The CAS is a modification of the VAS (McGrath et al. 1996; Miro and Huguet 2004). It is a simple and validated (McGrath et al. 1996) tool for measuring pain intensity that can be used for children aged 5 years and older. Because of children's cognitive development and the relative abstractness of the VAS format, modifications specifically for children have been made to the VAS. The simplest change is the rotation of the axis 90 degrees so that the child reads it in the vertical plane. This is based on the assumption that children's vertical quantification abilities precede horizontal quantification abilities (Johnston 1998). A final modification is the addition of colour, which varies in intensity, light pink to deep red (McGrath et al. 1996).

The CAS consists of a 14.3 cm long triangular shape varying in width and hue from 1.1 cm and light pink at the bottom to 3.0 cm and deep red hue at the top. *A plastic marker slides along the scale* to provide a pain rating along a continuum from the bottom to the top of the scale. On the opposite side of the CAS is a corresponding 0 to 10 numerical scale (from which the clinician takes a measurement not available to the child). The CAS is contained on a plastic card (17.5 x 2.5 cm)

McGrath et al. (1996) reported that the CAS was a valid tool for measuring pain intensity in children and adolescents aged 5 – 17 years. They also found that the CAS was easier to administer and score than the VAS in healthy children and those with recurrent headache (aged 5 to 16 years) suggesting that CAS may be more practical for routine clinical use in children. The manufacturer of CAS recommended that during pain assessment the sliding marker on the CAS be placed at the bottom of the scale (McGrath et al. 1996). This may influence the child's response especially where the child has no pain or is not in so much pain. Children may want to move the marker to please the person evaluating their condition.

From the foregoing, it is obvious that there is no specific means of assessing pain in children. However, a more quantifiable method of pain assessment in children may be expensive, time consuming and are impractical. The CAS provides children with the opportunity to rate their pain perception themselves; thereby it gives measure of pain intensity in children that reflects what the child experiences. The addition of markers along the line makes the CAS more easily scored than the traditional VAS.

The CAS is straightforward to use and does not require further measurement by the clinician. Additionally, it is inexpensive and can be easily administered. Moreover, the introduction of colours makes the CAS more children friendly than the VAS. Furthermore, the numerical ratings on the back of CAS enable researchers to quickly determine the number that represent a child's pain intensity. In view of these advantages the CAS was used in this research.

### **3.5 Methods of Assessing Muscle Strength (Torque)**

There are few studies that have reported muscle strength measurements in children with HMS. Therefore, further work on muscle strength assessment in children with HMS is required. This section examines issues concerning muscle strength assessment. It also discusses methods of evaluating muscle strength in children.

Measurement of muscle strength is an integral part of physiotherapy assessment of patients (Trudelle-Jackson et al. 1994). Accurate measurement of muscle strength is important for identifying strength deficits and documenting changes in performance as a result of interventions (Vermeulen et al. 2005). Methods of measuring muscle strength include manual muscle testing (Dvir 1997; Trew and Everett 2001; Bohannon 2002), use of various hand-held force myometers (Bohannon and Andrews 1987; Seagraves and Horvat 1995; Reinking et al. 1996; Engelbert et al. 2003) and computerised isokinetic muscle testing (McNair et al. 1996; Reinking et al. 1996; Pincivero et al. 2003). Manual muscle testing (MMT) is probably the most widely used method (Trew and Everett 2001; Bohannon 2002). Evidence indicates that hand-held myometers may yield more precise measurements and are more sensitive to small changes in strength than MMT (Noreau and Vachon 1998). The following section discusses different types of muscle contraction. The strengths and weaknesses of some methods of muscle testing are then examined in detail.

#### **3.4.5 Types of Muscle Contraction**

Muscle strength can be assessed isometrically or isotonically. Isometric contraction occurs when there is no visible change in the length of the contracting muscle (Norkin and Lanvangie 1988). Isotonic contraction takes place when there is movement of one or more of the bones to which the contracting muscles are attached (Trew and Everett 2001). Isotonic contraction can be divided into concentric and eccentric muscle activities. In concentric contraction, the contracting

muscle shortens and movement of bones and joints occurs (Trew and Everett 2001). During concentric contraction the muscle force generated is less than during isometric contraction (Norkin and Lanvange 1988; Trew and Everett 2001). This is because more cross bridges are formed during isometric contraction than isotonic activity. In eccentric muscle contraction the muscle undergoes lengthening and the external force is greater than that generated by the active muscle (Norkin and Lanvange 1988; Trew and Everett 2001). The maximum force generated by the contracting muscle is higher than under concentric and isometric conditions. It is believed that unfamiliar, high force eccentric contraction causes more fatigue, pain and muscle damage than concentric or isometric activities (Trew and Everett 2001).

Maximal isometric muscle contractions provide an index of skeletal muscle performance. Isometric muscle testing is recommended for patients with muscle weakness, who have been diagnosed as having a condition that leads to progressive muscle weakness, or who are recovering from musculoskeletal injury or corrective surgery (Amundsen 1990). Isometric muscle testing has a range of advantages (Amundsen 1990). It is easier to provide good stabilisation during testing. Effective stabilisation isolates the muscle group being tested, eliminates substitution and minimises the inhibition caused by unnatural joint traction or compression forces that can occur during dynamic testing. Additionally, isometric muscle testing produces less systemic fatigue than isotonic testing so that more muscles can be tested in a given session (Amundsen 1990). Moreover, isometric muscle testing is preferred where movement or muscle contraction causes pain. Isometric muscle contraction is necessary in the presence of joint contracture or painful arcs of joint motion. Lastly, isometric testing helps to distinguish between contractile and noncontractile tissue pathology. Isometric strength has to be expressed in torque to give accurate predictions concerning functional performance. In view of the numerous advantages that isometric muscle contraction/testing has, it was used for muscle torque assessment in this study.

Muscle strength testing can be affected by a variety of anatomical, physiological, mechanical and methodological factors such as age, gender, body mass, moment arm and joint angle (Smidt and Rogers 1982). Muscle strength has been reported in many ways such as in pounds or kilogrammes of force (Stuberg and Metcalf 1988, Rudelle-Jackson et al. 1994) and Newtons (Karner et al. 1998). Additionally,

Sykanda et al. (1988) reported muscle strength in relation to subjects' height. Strength has also been examined relative to the moment arm or length (torque) (Merlini et al. 1995). Effgen and Brown (1992) suggested that normative values of muscle performance may be given in terms of torque rather than in force. According to Effgen and Brown (1992) when muscle performance is reported in terms of torque, lever arm length (length of the limb or limb segment acting on the myometer) between subjects can be accounted for.

The length of the muscle, the lever arm, the type of contraction (Amundsen 1990) and the subject's body mass can cause very large differences in the muscle force output. Torque is the phenomenon that causes movement of the limb segment (Amundsen 1990). Torque values are determined by multiplying the muscle force by the length of the subject's limb (perpendicular distance between the point of application and joint axis) (Sloan 2002). Because of the advantages that muscle torque has over muscle strength, the term 'muscle torque' is used henceforth in this thesis. Some methods of muscle testing are discussed in detailed below.

#### **3.4.6 Manual Muscle Testing**

Manual muscle testing (MMT) is a means of testing and grading muscle strength based on gravity and manually applied resistance. MMT is based on use of motion, gravity and manually applied resistance by the examiner to test and determine muscle performance. The muscles are graded 0 to 5, where 0 is the least strength and 5 indicate normal muscle performance.

Florence et al. (1984) reported an excellent test-retest repeatability ( $ICC = 0.95$ ) and interrater repeatability ( $ICC = 0.90$ ) of MMT in children aged 5 to 15 years with muscular dystrophy. MMT testing is simple and inexpensive. In addition, it is believed that MMT provides a quick and global impression of muscle performance of an individual (Dvir 1997). However, it is a subjective means of assessment that lacks sensitivity and responsiveness when used to quantify muscle performance (Bohannon 2002). MMT does not give quantifiable data, it is prone to bias, and may therefore be unsuitable for use in children diagnosed with HMS.

### **3.4.7 Isokinetic Dynamometry**

Isokinetic dynamometers are stationary, electromechanical devices that control the velocity of a moving body segment by resisting the patient's effort such that the body segment cannot accelerate beyond the preset angular velocity. Isokinetic dynamometers can be used to measure muscle torque produced during isometric contractions. They are especially helpful in examining the performance of large and relatively strong muscle groups. Muscle groups acting at the knee, back, and to a lesser extent the elbow and shoulder are the ones most frequently tested with isokinetic devices.

Isokinetic systems are constructed primarily for use in adults, but they can be used in children who are large enough to fit the various components. The components of isokinetic system could be modified or smaller ones could be developed to meet the size of children. Although it has been used for assessing knee muscle torque in children as young as 6 years old (Backman & Oberg 1989; Merlini et al. 1995; Wiggin et al. 2006), isokinetic dynamometers are expensive and their use in children lacks a standardised protocol making repeatability of results difficult (Wiggin et al. 2006).

Bohannon (1987) believed that isokinetic dynamometers underestimate knee extension torque when measured with the subject's limb in a gravity resisted position, while knee flexion torque is overestimated with the subject's limb in a gravity assisted position. Additionally, there may be torque overshoot with the use of isokinetic dynamometer as the speed of the dynamometer may be exceeded by subjects being tested (Bohannon 1987). In view of the above limitations, it was not used for assessing muscle torque of children diagnosed with HMS in the present study.

### **3.4.8 The Fixed-Load Cells**

The fixed-load cell provides subjects with adequate stabilisation and it is more convenient for subjects during testing (Amundsen 1990).

A fixed-load cell can be used for assessing any muscle group in the human body. It is believed that it provides very sensitive measures for different muscle groups (Amundsen 1990) and does not depend on the strength of the examiner. This device

is expensive, large and cumbersome. This makes it unsuitable for clinical use. Therefore, it was not used for measuring muscle torque in children diagnosed with HMS.

### **3.4.9 Myometers (Dynamometers)**

Different types of myometers have been developed and used for muscle testing both clinically and in research studies (Bäckman et al. 1989; Effgen and Brown 1992; Seagraves and Horat 1995; Vermeulen et al. 2005). Myometers can be hand-held or fixed in nature and may be mechanically or electrically operated. Examples include spring gauges (Balogun and Onigbinde 1992), hand-held myometer (HHMs) (Bohannon and Andrews 1987; Stuberg and Metcalf 1988; Deones et al. 1994; Stratford and Balsor 1994; Trudelle-Jackson et al. 1994) and the Hammersmith myometer (Hyde and Goddard 1983). At the moment, there is no consensus on the exact name for these strength assessment tools as they are often referred to as 'myometers' (Backman et al. 1989; Sloan 2002; Engelbert et al. 2003; Engelbert et al. 2004; Engelbert et al. 2006) or 'dynamometers' (Reilly and Walsh 2005; Vermeulen et al. 2005) by researchers and authors. Therefore, in order to avoid confusion, the term 'myometer' is used throughout this thesis. The strengths and weaknesses of myometers are considered below:

#### **3.4.9.1 Hand-Held Myometers (HHMs)**

Hand-held myometers as the name implies, are grasped in the hand of the examiner during testing (Bohannon 1987). They are portable devices, placed between the examiner's hand and the patient's body, that measure mechanical force. Patients are typically asked to push against the examiner in a maximal isometric contraction ('make' test), or hold a position until the examiner overpowers the muscle producing an eccentric contraction ('break' test). The torque measured by the myometer is affected by the method of applying the resistance, the patient's body position in relationship to gravity, joint angle, myometer placement on the patient, stabilisation and the examiner's strength (Andrew et al. 1996).

HHMs are quantitative, inexpensive, easy to use and require less space in comparison to isokinetic devices (Reilly and Walsh 2005). A good to excellent test-retest repeatability (ICC range = 0.75 to 0.99) was observed when upper and lower limb muscle torque was measured with a HHM (Effgen & Brown 1992) in children

aged 9-17 years with meningocele. HHMs are prone to error due to off-centre loading, difficulties in subjects' positioning and stabilisation and limitations in the strength and experience of the examiners (Andrew et al. 1996; Reilly and Walsh 2005).

Some HHMs have a maximum capacity of 27.2kg (Stuberg and Metcalf 1988); therefore, their use in older children with larger muscle groups that are likely to generate high isometric muscle torque may be limited. Additionally, the mechanical spring in the spring-based myometer may become fatigued overtime and lead to inaccurate torque measurement (Bohannon and Andrews 1989). Therefore, due to these limitations, HHM was not be used for muscle torque assessment in this study.

#### **3.4.9.2 Fixed Myometers**

Fixed myometers are static force gauges specifically designed for muscle torque assessment in clinical research. As the name implies, they are fixed to a stable object or frame (Bohannon 1987) during the testing procedure. An example of the fixed myometer is the digital myometer manufactured by MIE Medical System Ltd, UK. It consists of a transducer between 2 sets of straps. One strap is placed around the subject's limb, while the other is attached to a fixed point. The MIE myometer is electrically controlled and has a displaying unit where the force measured is displayed. The MIE myometer can be used for assessing large muscle groups with minimal discomfort to subjects and the examiner.

Test-retest repeatability of the MIE digital myometer has been reported to be excellent in healthy children (ICC = 0.93) and good in children with cerebral palsy (ICC = 0.79) (Seniorou et al. 2002). Similarly, Van der Linden et al. (2004) have also demonstrated a good to excellent test-retest repeatability of the MIE myometer in healthy children (ICC range, 0.77 to 0.85) and children with cerebral palsy (ICC range, 0.75 to 0.83). The problem of stabilisation associated with HHMs can be overcome with the use of the MIE myometer as its stability does not depend upon the examiner (Bohannon 1987). In addition, it does not depend on the strength and experience of the examiner.

In conclusion, the methods of measuring muscle strength include manual muscle testing (Bohannon 2002), hand-held myometers (Engelbert et al. 2003) and isokinetic dynamometers (Wiggin et al. 2006). While MMT is probably the most widely used method (Trew and Everett 2001; Bohannon 2002), evidence indicates that muscle strength testing using measuring instruments such as hand-held myometers may be more precise and sensitive to small changes in strength than the MMT (Noreau and Vachon 1998). As a result, the MIE myometer was used for muscle torque assessment in this study.

### **3.5 Quality of Life**

QoL is believed to be a unique personal perception, denoting the way that individual patients perceive and react to their health status (Gill and Feinstein 1994). QoL can be suitably measured by asking the patients directly to rate their 'overall' quality of life and the importance of individual items affecting their QoL.

Health-related quality of life (HRQOL) is the impact of health and illness on the individual's QoL (Eiser and Morse 2001). Although the terms HRQOL and QoL have different meanings, they have been used interchangeably. It is believed that the term QoL has been used ubiquitously (Gill and Feinstein 1994) and is commonly used in paediatric rheumatology (Press et al. 2002; Janse et al. 2005; April et al. 2006). According to Feinstein et al. (1986) HRQOL assessment in clinical research and in clinical practice can be used to determine compensation and treatment plans and to indicate changes in a patient's response to an intervention.

HRQOL is more focused than overall QoL, and can include a wide range of dimensions which include (1) signs and symptoms of disease, (2) performance of basic physical activities of daily life (ADL), (3) performance of social roles, (4) emotional state, (5) intellectual functioning and (6) general satisfaction and perceived well-being (Bergner 1989). QoL is made up of three components (Jette 1993) – physical, psychological and social functioning. These components are discussed below.

#### **a) Physical Functioning Component**

Physical function encompasses the performance of daily activities required to sustain the individual (Jette 1993). As described by Jette (1993), the physical functioning component of QoL includes performance of basic life activities such as



dressing, bathing, and walking and more complex life activities such as mental preparation, shopping, and transportation.

**b) Psychological Functioning Component**

The psychological functioning component of QoL consists of various cognitive, perceptual and personality traits of the individual (Jette 1993). Examples are self-esteem, attitude toward body image, anxiety and depression (Jette 1993).

**c) Social Functioning Component**

Social function is viewed as the interaction of the individual within a larger social context or structure such as social activity, including participation in recreational activities and clubs, social interaction, telephoning or visiting relatives or friends (Jette 1993).

It is believed that the three components interact with each other in the framework; alterations in one component may affect the others within the model (Jette 1993). The ultimate goal of providing physiotherapy services to patients with chronic disease is to improve their functional status and level of overall QoL (Jette 1993). Physiotherapy research sometimes focuses on improvements in impairments in evaluating the effectiveness of patients' rehabilitation without paying attention to QoL in the patients. Researchers in rheumatology have suggested that QoL measures should be added to all clinical trials in rheumatology to complement anthropometric, clinical, and laboratory data (Bell et al. 1990). This is probably because physical measures alone cannot be relied upon to determine the effectiveness of treatment intervention on patients (Gong et al. 2007).

Various QoL measures have been developed for assessing children with chronic conditions. The selection of a standardised instrument depends on several important factors, including (1) selected dimensions to measure, (2) psychometric properties, and (3) practicality. Some QoL measures in children are examined below:

**3.5.1 Functional Status II Revised (FSIIR)**

FSIIR is a questionnaire that was developed for assessing a child's health status. It was designed for children aged 0-16 years. It has 8 domains (communication, mobility, mood, energy, play, sleep, eating, and toileting), and either 43-items (long version) or 14-items (short) (Stein and Jessop 1990). The questionnaire also

contains sociodemographic information, diagnosis, duration of illness, traditional morbidity measures (number of days in bed and number of days in hospital), and parental assessment of current stability of the condition.

FSIIR is a comprehensive tool that can be completed within 30 minutes (Stein and Jessop 1990). It is inexpensive and can be administered by a lay interviewer. Moreover, FSIIR spans the entire childhood age range. On the other hand, it relies exclusively on parental reports. It has been demonstrated that mothers of children with juvenile arthritis rated their children's perceived competence more negatively than the children themselves (Ennett et al. 1991). Similarly, when parents were asked to rate the QoL perception of their children, it was found that they reported lower values than the children themselves (Bruil 1999). Since FSIIR is based on parental reports, there is the tendency that the reports provided by parents on their children may not reflect the QoL perception of their children. Hence, it was not used by the investigator in this research.

### **3.5.2 Paediatrics Quality of Life Questionnaire (PedsQL)**

The paediatrics quality of life questionnaire or inventory was derived from the Paediatric Cancer Quality of Life inventory (PCQL) and developed for parents and patients with cancer and or chronic paediatric conditions (age range, 8-18 years) (Varni et al. 1998). The PCQL was developed as a standardised assessment instrument to assess systematically pediatric cancer patient's QoL outcomes (Varni et al. 1999). PedsQL has been used to assess the generic core and disease/symptom specific QoL in these patients (Varni et al. 1998). It is non-categorical in nature i.e. can be used across all paediatric chronic health conditions. PedsQL measures children and their parents' perceptions in terms of the impact of the disease and treatment on physical, psychological and social functioning and disease/treatment-specific symptoms.

It consists of 23 multidimensional modules encompassing the following: 1, Physical functioning scale (8 items); 2, emotional functioning scale (5 items); 3, social functioning scale (5 items); and 4, school functioning (scale 5 items). Each module is answered with a 5-point Likert scale across both child and adolescent self report for ages 8-15 years (0 = 'never a problem', 1 = 'almost never a problem', 2 = 'sometimes a problem', 3 = 'often a problem', 4 = 'almost always a problem').

The PedsQL is made up of two versions: The patient self-report and parent proxy-report versions (Varni et al. 1998). Each version is made up of the child (age range, 8-12 years) and adolescent (age range, 13-18 years) forms. PedsQL provides opportunity for a child to self-report the impact of disease condition on their health status. This questionnaire has a limitation like other QoL measures in children. It is a five point ranking questionnaire. Therefore, it is possible that responses of children on the scale might be centred mainly on the middle response.

On the other hand the questionnaire has the following advantages over other QoL measures in children. First, it covers all the necessary domains and can be completed within 5-10 minutes. Secondly, PedsQL is applicable to a range of chronic paediatric health conditions. Additionally, it is inexpensive and easy to use. Moreover, the validity and responsiveness of the PedsQL 4.0 module has been demonstrated in paediatric rheumatology by Varni et al. (2002) to be excellent (ICC range = 0.8 to 0.9). In view of the advantages of PedsQL hence it was used to assess QoL in children in this study.

### **3.6 Gait Analysis**

Gait analysis is a broad term that can refer to many different methods of evaluating an individual's walking pattern (Rose et al. 1991). One of the major purposes of the rehabilitative process is to help patients achieve a high level of functional independence within the limits of their particular impairments. Human gait is one of the basic components of independent functioning that is commonly affected by either disease processes or injury.

Gait analysis is a complex activity and may be used to identify the mechanisms causing dysfunction (Mueller et al. 1995). It can also be used for classifying the severity of disability, prediction of patient's future status and for description of the differences between a patient's performance and the parameters of normal gait (Mueller et al. 1994; Von Schroeder 1995). Additionally, gait can also be used for assessment of the effects of treatment interventions (Damiano et al. 1995; Selby-Silverstein et al. 1997).

Gait parameters can be classified into kinematics and kinetics. Kinematics is used to obtain information on time and distance gait variables as well as motion patterns (Norkin 2001). Kinetics is used to determine the external and internal forces during walking (Norkin 2001). Equipment used in gait analysis may either be simple or complex (Norkin 2001).

Although it has been suggested that abnormal joint biomechanics may be found in individuals with HMS due to joint laxity, this has not been investigated (section 2.4.3). Alter biomechanics may affect the kinematic patterns of the knee joint during walking. Therefore, this thesis focused on kinematic gait analysis.

### **3.6.1 Qualitative Gait Analysis**

Gait kinematics can be carried out qualitatively and quantitatively. The most common method used in the clinic is a qualitative gait analysis. This method requires a small amount of equipment and a minimal amount of time (Norkin 2001). The primary variable that is assessed in qualitative kinematic gait analysis is joint displacement, which includes a description of patterns of movement, deviations from normal body postures, and joint angles at specific points in the gait cycle. Some methods of qualitative assessment are described below.

#### **a) Observational Gait Analysis**

Observational gait assessment (using the naked eye or video images) is the most commonly used clinical method of performing kinematics qualitative analysis (Toro et al. 2003). It is frequently used by physiotherapists to assess a patient's gait and it forms a major aspect of physiotherapy practice. Considerable training and constant practice are necessary to develop the skills that are needed for performing any observational gait analysis (Norkin 2001).

Observational gait analysis requires little or no instrumentation, it is inexpensive to use, and yields general descriptions of gait variables (Norkin 2001). However, it is subjective and as a result its validity, repeatability, sensitivity, and specificity compared to more objective instrumented gait analysis are questionable (Eastlack et al. 1991).

**b) Videotape Gait Analysis**

Video analysis is an excellent tool that can be used to supplement observational gait analysis. It allows the clinician more time to observe gait by reviewing the information repeatedly without the effect of patient fatigue (Rose et al. 1991). The most practical system consists of a camera-recorder (camcorder), to do the videotaping, and a separate VCR to replay the tapes.

A videotape providing slow motion and stop-frame facilities may be used to visualise events that are too fast for the unaided eye. Video recording of gait has become popular in clinical settings (Toro et al. 2003) due to its ability to overcome some of the problems associated with naked eye evaluation of gait, such as the speed of movements and only seeing the gait cycle once. Whittle (1991) believed that it confers the following advantages: it reduces the number of walks a subject needs to do, it makes it possible to show subjects exactly how they are walking, and it makes it easier to teach visual gait analysis to someone else on a monitor.

Visual gait analysis using videotape is a subjective method but it is easy to use. Also, objective data can be derived from the general gait parameters (cadence, stride length and velocity) (Whittle 1991). Krieb et al. (1985) demonstrated a good test-retest repeatability (ICC = 0.73) and moderate interrater repeatability (Pearson product-moment correlation = 0.6) of observational gait analysis in highly trained clinicians using stop-motion video recording.

**c) Ambulation Profiles or Scales**

The ambulation profiles and rating scales constitute gait analyses that often include both qualitative (such as observational) and quantitative (such as time and distance) measures. Profiles are used for a variety of reasons, for example they can be used to determine patient's need for assistance and screening for identification of patient's need for physiotherapy (Harada et al. 1995). The following are examples: The functional Ambulation Profile (FAP), the Iowa Level of Assistance Score, the Functional Independence Measure (FIM) and the Functional Independence Measure for Children. The advantage of some of these profiles is that subordinate gait skills such as standing balance may be assessed in individuals who may not be able to walk unassisted.

### **3.6.2 Quantitative Gait Analysis**

Quantitative kinematic gait analyses are used to obtain information on time and distance variables as well as motion patterns (Norkin 2001). The data obtained through these analyses are quantifiable and therefore provide clinicians with baseline data that can be used to plan treatment programmes and to assess progress towards or attainment of goals. Some methods are discussed below.

#### **Footswitches**

Footswitches are used to record the timing of gait and can be used to determine walking speed (cm/s), cadence (steps/min) and mean stride length (cm) (Whittle 1991). Footswitches are most conveniently used with shoes, although suitably designed ones may be taped directly beneath the foot. Small switches may also be mounted in an insole, and worn inside the shoe. Assessment with footswitches is quick and easy to administer. It is safe and non threatening even to persons with severe gait disabilities (Whittle 1991). Also, it can be used to assess large numbers of patients while providing measurements of mean walking speed, cadence, and stride length (Fransen et al. 1997). Additionally, only a few trials are needed to achieve good measures with footswitches.

On the other hand, footswitches may be exposed to very high forces, which may cause problems with repeatability of data collected. Fast walking speed provided greater test-retest repeatability measurements than did gait at a normal self-selected walking speed (Fransen et al. 1997). However, repeatability increased markedly from the first intersession analysis to the second. Thus, footswitches may not be responsive to change at normal walking speed.

#### **Electrogoniometer (ELGON)**

An electrogoniometer (ELGON) is a device for measuring joint angles during walking. The output of an electrogoniometer is usually plotted as a chart of joint angle against time. However, if measurements have been made from two joints, the data may be plotted as an angle/angle diagram.

An ELGON system has the advantage of being relatively inexpensive and it provides immediate feedback (Chao et al. 1983). An ELGON system was successfully used for repeated measurements of the gait cycles of children with cerebral palsy, in a study into the effect of electrical stimulation on the lower limb kinematics in these

children (Hazlewood et al. 1995). The limitations of ELGON systems include that they are difficult to align properly on the joint. The attachment mechanisms of the ELGON can encumber the subject and affect the movement pattern (Chao et al. 1983). Given these limitations an ELGON was not used for gait analysis in the present study.

### **VICON Camera System**

Quantitative gait analysis using a computer-aided motion analysis system such as (VICON) is commonly being used as a valuable tool in clinical and research settings for quantitative kinematics data collection (Kadaba et al. 1989; Gorton et al. 1997; Stansfield et al. 2001; Schache et al. 2002; Orendurff et al. 2002; Thambyah et al. 2004). It is made up of infrared cameras located around a walkway. The cameras are connected to a computer that is used for data capture during walking. The VICON system is used with lightweight reflective markers, which are usually attached to specific bony landmarks. Data from it can be processed using appropriate software.

The VICON system is expensive and requires training as it may be associated with error in reflective marker placement that can result in significant skin movement. However, data from the VICON system can be useful as it can provide information on many joints at the same time. Additionally, the problem of having subjects to walk many times on a walkway when using visual estimation is not associated with VICON system because captured data can be reviewed by the clinician during the the process of data analysis. Furthermore, both within-day and between-days test-retest repeatability of sagittal knee motion were found to be excellent in healthy adults (Coefficient of multiple correlation range =  $0.994 \pm 0.05$ ,  $0.990 \pm 0.009$  by Kadaba et al. (1989)). In comparison with other methods of gait analysis the VICON system has some disadvantages as stated above. However, this is the first time that quantitative gait analysis is being investigated in children with HMS, and due the availability of the system, it was used in the present study.

### **3.7 Conclusion**

In conclusion, it is clear that there are a wide range of qualitative and quantitative methods of assessing GJL. At present there is no universally accepted '*gold standard*' for defining both GJL and HMS. The Beighton and Brighton criteria are the most frequently used in both clinical and research settings for diagnosing HMS.

Furthermore, the diagnostic tools currently used for diagnosing HMS only consider the ROM and pain at some joints, and fail to consider other possible symptoms that may be associated with this condition. Therefore, this provides a rationale for a cross-sectional study to identify a range of factors that may be associated with HMS in children. Consequently, this research will determine the neuromuscular performance, functional ROM and QoL characteristics of children diagnosed with HMS.

Because impaired joint proprioception has been identified as a key factor that may be associated with HMS, the next chapter discusses issues relating this outcome.



## **CHAPTER 4 : JOINT PROPRIOCEPTION**

### **4.1 Introduction**

In section 2.5, it was stated that impaired joint proprioception may be associated with HMS. This chapter describes the neurophysiology of proprioception and the influence of age, gender and joint laxity on proprioception. Additionally, the problems in clinical assessment and methods of assessing joint proprioception in clinical research are discussed.

Proprioception was introduced by Sherrington (1906) as the ability to sense the position and movements of limb segments. This term accommodates all senses other than pain and temperature derived from the muscles and their accessory organs. Since proprioception was introduced by Sherrington, many definitions have evolved as summarised in Table 4.1. Barrack et al. (1983a) used the term joint position sense (JPS) to describe proprioception as the threshold of detection of passive motion and ability to reproduce angles to which it was passively placed. Their definition of JPS was a combination of joint kinaesthesia (JK) and JPS as defined by Ludon (2000) and Grob et al. (2002).

The terms 'proprioception', 'kinaesthesia' and 'joint position sense' are often used interchangeably (Gilman 2002; Reimann and Lephart 2002) without full regard to the different meanings. There is lack of agreement in the use of the terms JK and JPS. Joint position and kinaesthetic senses are components of the proprioceptive senses. In this thesis, JPS refers to the ability of a subject to reproduce an angle at which a joint had previously been placed (Corrigan et al. 1992). JK is the ability of a subject to perceive movement when the angle of the joint is altered slowly (Corrigan et al. 1992).

To avoid confusion in terms of the meaning of 'joint proprioception', therefore, in this thesis, joint proprioception refers to a combination of joint kinaesthetic and position senses.

**Table 4.1: Summary of the definitions of joint proprioception**

Author	Term used	Definitions
Sherington (1906)	Proprioception	Ability to sense the position and movements of limb segments relative to one another
Barrack et al. (1983a)	JPS	Threshold of detection of slow, constant passive motion and ability to reproduce angles to a joint which was passively placed
Corrigan et al. (1992)	JK	Ability of a subject to perceive movement when the angle of the joint is altered slowly
Kalaska (1994)	Proprioception	Conscious awareness of limb movement and position
MacDonald et al. (1996)	Proprioception	Sensory afferent-feedback mechanism
Voight et al. (1996)	Proprioception	Cumulative neural input to the central nervous system from specialised nervous endings called mechanoreceptors
Borsa et al. (1997)	Proprioception	A specialised variation of the sensory modality of touch and encompasses the neurosensitivity of joint motion and position
Lattanzio et al. (1997)	Proprioception	The inborn kinaesthetic awareness of body posture including movement, tension and change equilibrium
Fermerey et al. (2000)	Proprioception	Sensory information about kinaesthesia and joint position
Gurney et al. (2000)	Proprioception	Awareness of posture, movement and changes in equilibrium and the knowledge of position, weight and resistance of objects in relation to the body
Ludon (2000)	JPS	Ability to sense joint in space
Pincvero et al. (2000)	Proprioception	Conscious awareness of limb position and movement
Tsang and Hui-Chan (2003)	Proprioception	Detection of limb position and movement in absence of vision

JK = Joint kinaesthesia; JPS = Joint position sense

## **4.2 Neurophysiology of Joint Proprioception**

Mechanoreceptors are responsible for proprioception. According to Grigg (1994) mechanoreceptors are specialised sensory receptors that transduce the mechanical events occurring in their host tissues into neural signals. They also help in reflex regulation of all types of muscular contraction, coordinate movement and posture, balance and the reflex muscular defence of joints against potentially harmful mechanical forces (Evarts 1981).

Stillman (2000) believed that the proprioceptive system serves the following functions:

1. Reflexly contributes to coordinate posture and movement.
2. Reflexly contributes to protection of joints against potentially harmful mechanical forces.
3. Collects senses other than pain and temperature which may be experienced within the musculoskeletal system.
4. Modulates the influence of one afferent signal on another. For example, in the gate control theory of pain, part of the proprioceptive input into the spinal cord, acting via inhibitory interneurons, may diminish pain.

### **Proprioception and Sensory Interaction**

It is acknowledged that all skeletal motor activities involve some central processing of proprioceptive afferent information (Gilman 2002; Reimann and Lephart 2002). Stillman (2000) stated that rapid movements are least dependent on proprioception. In slower movements the rapidly conducting large diameter proprioceptive afferents provide the central processing centres, especially the cerebellum, with information for the purpose of monitoring and processing the on-going movement.

Flament et al. (1996) observed that the cerebellum, aided by the prefrontal cerebral cortex is involved during the learning of new skills. Patients with cerebellar disorders were demonstrated by Cody et al. (1993) to be less proficient than a group of control subjects who attempted to replicate a computer-generated saw-tooth movement pattern using wrist flexion-extension. In these patients, Cody et al. (1993) reported that movement control was further disturbed when observation of the movement was briefly interrupted. Therefore, the cerebellum may be involved in central processing of proprioception.

The word 'joint' in JK and JPS should not be interpreted as meaning that the receptors responsible for these sensations are located entirely in the joints. Most of the receptors are likely to reside outside the joint, particularly in the surrounding muscles (Grigg 1994; Gilman 2002; Reimann and Lephart 2002). The types and locations of these receptors are discussed below.

#### **4.3.2 Joint Proprioceptors**

Sensory receptors responsible for joint proprioception are located in the surrounding muscles, articular capsule and skin. Muscular receptors consist of muscle spindles, Golgi tendon organs, corpuscular receptors and free nerve endings. Articular cartilage has no nerve endings. Synovial tissue lining the joint cavity contains only free nerve endings, and all other joint tissues. The synovial sheaths surrounding tendons and ligaments contain both free nerve endings and corpuscular receptors. Approximately 80% of articular receptors are free nerve endings (Heppelmann et al. 1988). Free nerve endings in the joint are mostly highly threshold mechanonociceptors or polymodal nociceptors. The cutaneous receptors are made up of merkel discs, ruffini endings, meissner corpuscles, lamellated corpuscles, hair follicles and free nerve endings (Gilman 2002). A majority of cutaneous receptors are free nerve endings (and hair follicle receptors in hairy skin). Detailed accounts of the proprioceptors are provided by Barrack and Skinner (1990), Grigg (1996), Hogervorst and Brand (1998), Stillman (2000) Tortora and Grabowskwi (2003), Lindsay et al. (2004) and Snell (2006). A summary of joint proprioceptors and their location is provided Table 4.2.

##### **4.3.2.1 Adaptability of proprioceptors**

One of the characteristics of most proprioceptors is adaptation (Tortora and Grabowskwi 2003). This is a decrease in amplitude of a receptor potential during a maintained, constant stimulus. Adaptation results in a decrease in the frequency of nerve impulses in the first-order neuron during a prolonged stimulus. As a result of adaptation, the perception of a sensation may fade or disappear even though the stimulus persists. Proprioceptors have different adaptive properties based on their response to a continuous stimulus (Lephart et al. 1992; Tortora and Grabowskwi 2003; Snell 2006). Rapidly adapting proprioceptors adapt very quickly to the onset of a continuous stimulus (Lephart et al. 1992). Examples of these are Pacinian corpuscles, Meissner corpuscles and lamellated corpuscles. On the other hand the slowly adapting proprioceptors such as Ruffini endings and Golgi tendon organ

adapt slowly and continue to trigger nerve impulses as long as the stimulus persists. The summary of the adaptability of joint proprioceptors is illustrated in Table 4.2. It is acknowledged that the information provided on the classification and characteristics of the joint receptors were obtained from textbooks (Tortora and Grabowski 2003; Snell 2006) as access to the original work where they were first reported was beyond the scope of the present study. Therefore, this information should be treated with caution as it might not have been interpreted correctly in the textbooks.

**Table 4.2: Summary of joint proprioceptors and their location**

<b>Author(s)</b>	<b>Receptors</b>	<b>Location</b>	<b>Adaptability</b>
Burke et al. (1993); van Willigen et al. (1993); Wilson et al. (1997); Stillman (2002); Snell (2006)	Muscle spindles	Bellies of most skeletal muscles	Slow, but the primary endings are also partly rapidly adapting
McCloskey (1987); Jamie et al. (1992); Bergenheim et al. (1996); Lephart and Reimann (2002)	Golgi tendon organs	Musculotendinous junctions, muscle bellies and tendons	Slow
Snell (2006)	Pacinian Corpuscles	Dermis, ligaments, joint capsules	Rapid
Lindsay et al. (2004); Snell (2006)	Meissener corpuscles	Dermal papillae of hairless skin	Rapid
Gilman (2002); Lindsay et al. (2004); Snell (2006)	Lamellated corpuscles	Deep in the dermis of hairless skin, joints	Rapid
Grigg (1996); Ochoa and Torebjork (1989); Schmidt (1996); Schaible and Schmidt (1996); Lobbenhoffer et al. (1996); Mense (1996); (Vallbo et al. 1999)	Free nerve endings	Epidermis and dermis of hairy and hairless skin, muscle bellies, tendons, joints, ligaments and connective tissues	Slow and rapid
Halata et al. (1985); Burke et al. (1988); Lephart et al. 1992); Snell (2006)	Ruffini endings	Dermis of hairy skin	Slow
Stillman (2000); Tortora and Grabowskwi (2003); Snell (2006)	Merkel discs	Epidermis of hairy and hairless skin	Slow
Stillman (2000); Snell (2006)	Hair follicle Receptors	Hairy skin	Rapid

#### **4.3.2.2 Sensation and functions of proprioceptors**

Proprioceptors help to convert mechanical deformation into a frequency-modulated neural signal that is transmitted via cortical and reflex pathways. These are responsible for signalling changes in a stimulus such as pressure or touch.

##### **(a) Muscle spindles**

Muscle spindles are mechanoreceptors that sense how far and how fast a muscle lengthens (Maier 1997). It has been suggested that when resistance is added to a contracting muscle, it results in an increased fusimotor discharge onto that muscle (Macefield et al. 1993). Voluntary isometric contractions of the tibialis anterior muscle at less than 3.2% of maximum were found to produce a response from 24 (92.3%) of 26 examined afferents in 90% of instances (Wilson et al. 1997). The peak spindle afferent discharge occurred shortly after the onset of muscle contraction (Burke and Gandevia 1993). Muscle spindle responses were observed during low intensity isometric contractions by Wilson et al. (1999) in the spastic hand muscles of stroke patients.

Based on the above information on muscle spindle, it seems that muscle spindles actively contribute to proprioception during isometric muscle contraction, even when this is weak.

##### **(b) Golgi Tendon Organs (GTOs)**

GTOs function mainly to signal active muscle tension (during muscle contraction) rather than passive tension (during passive stretching) (Jami 1992). Their response to brief or sustained muscle stretch is largely insignificant because their threshold is very high (Jami 1992; Stillman 2000). It is believed that GTO contributes towards the greater proprioceptive acuity associated with active as compared to passive JPS tests (Colebatch and McCloskey 1987). According to Bergenheim et al. (1996), sensing of active versus passive muscle stretch depends on the different sensitivities of the muscle spindles and GTO stretch receptors. Therefore, it seems likely that they have the capacity to respond to the same stimulus.

GTO's may also contribute to the senses of force and effort that accompany voluntary and, particularly, resisted muscle contractions (Gandevia and Burke 1992). This may help to enhance the perception of active JPS as compared to passive JPS. From the above it can therefore be assumed that afferent information from GTOs contributes to JPS senses when muscles surrounding the joint are active. This may be limited under passive muscle tension condition.

### **(c) Corpuscular Receptors**

Lamellated corpuscles sense vibration and pressure changes, but not constant pressure (Tortora and Grabowski 2003; Lindsay et al. (2004). Grigg et al. (1982) suggested that lamellated corpuscles detect external joint compression and increased intra-articular pressure. It seems that these receptors might also sense the most dynamic aspects of joint movements. Pacinian corpuscles are responsible for detecting vibration (Gilman 2000; Tortora and Grabowski 2003; Lindsay et al. 2004). Meissner corpuscles detect pressure, fine touch and slow vibration (Snell 2006). They are also responsible for texture and movement of held objects (Stillman 2002). Meissner corpuscles in the skin surrounding finger joints are believed to be sensitive to joint movements but not postures (Lindsay et al. 2004).

### **(d) Free Nerve Endings**

Mense (1996) reported that about 40% of free nerve endings are non-nociceptive pressure and contraction receptors. 40% are mechanical, chemical and/or thermal nociceptors, while 20% are non-nociceptive temperature receptors. Most articular free nerve endings are noxious and non-noxious pressure and movement sensors (Schaible and Schmidt 1996). The remainder are chemonociceptors. Most mechanoreceptive free nerve endings in normal joints are only stimulated by extreme joint movements and are probably not normally significant sources of proprioception (Schmidt 1996). However, like muscular free nerve endings when there is inflammation, a large proportion of the free nerve endings are sensitised by chemical substances produced during the inflammatory process (Grigg 1996; Stillman 2000). Consequently, this may result in impaired joint proprioception.

Afferent free nerve endings in the skin are touch and pressure receptors (Vallbo et al. 1999). Free nerve endings are high threshold nociceptors responding to mechanical, thermal or chemical stimulation, non-nociceptive cold and warmth endings. When single nociceptive afferents are stimulated, a sense of sharp,



stinging, pricking, burning or dull pain is evoked depending on the type of afferent and stimulus frequency (Ochoa and Torebjork 1989). Cutaneous free nerve endings are unlikely to play a part in JPS (Grigg 1996).

#### **(e) Ruffini Endings**

Ruffini endings facilitate transmission of capsular stretch to the receptors (Halata et al. 1985). They are responsive to static and dynamic tension applied in all directions within the plane of the structures in which they reside (Grigg 1996). The adapting endings in the posterior capsule of cat knees respond to increased intra-articular pressure (Ferrell 1987) and the posterior capsules of cats' hip respond to mechanical vibration (Aloisi et al. 1988). It has also been reported that a proportion of Ruffini endings in cats' knees have a spontaneous resting discharge (Ferrell 1980).

A study of the knee (Krauspe et al. 1992) confirmed that Ruffini endings discharge maximally at the extremes of joint movement. They are also active within the joint's midrange. Midrange articular afferent activity has been reported in the knee of cats, primates and dogs (Nade et al. 1987). The Ruffini endings located in skin can sense deep touch, pressure and the weight of static or moving objects held in the hand or placed elsewhere on the body. Receptors in the hairy skin on the back of the hand respond throughout the entire physiological range of finger movement. Ruffini endings in the skin over the dorsum of the wrist respond to metacarpophalangeal joint movements (Edin and Abbs 1991). They also play a significant part in proprioceptive acuity of the finger. However, because of the specialised function and innervation of the human hand, it may be difficult to assume that skin receptors have a similar proprioceptive role at the knee joint. Indirect evidence for a proprioceptive skin stretch mechanism operating outside the hand is provided in a study by Cohen et al. (1994).

Thus, it appears that the discharge frequency of the active receptors at each position throughout a joint's physiological range of movement is used by the sensory cerebral cortex when determining each joint position or each phase of a joint movement (Clark and Horch 1986). Based on the above findings, it is likely that articular Ruffini endings play some roles in joint position, movements and intra- and

extra-articular pressure. The Ruffini endings in the skin may also be responsible for joint proprioception.

#### **(f) Merkel Discs**

Merkel discs respond to pressure stimulation and help to define the shape of objects held in the hand.

#### **(g) Hair Follicle Receptors**

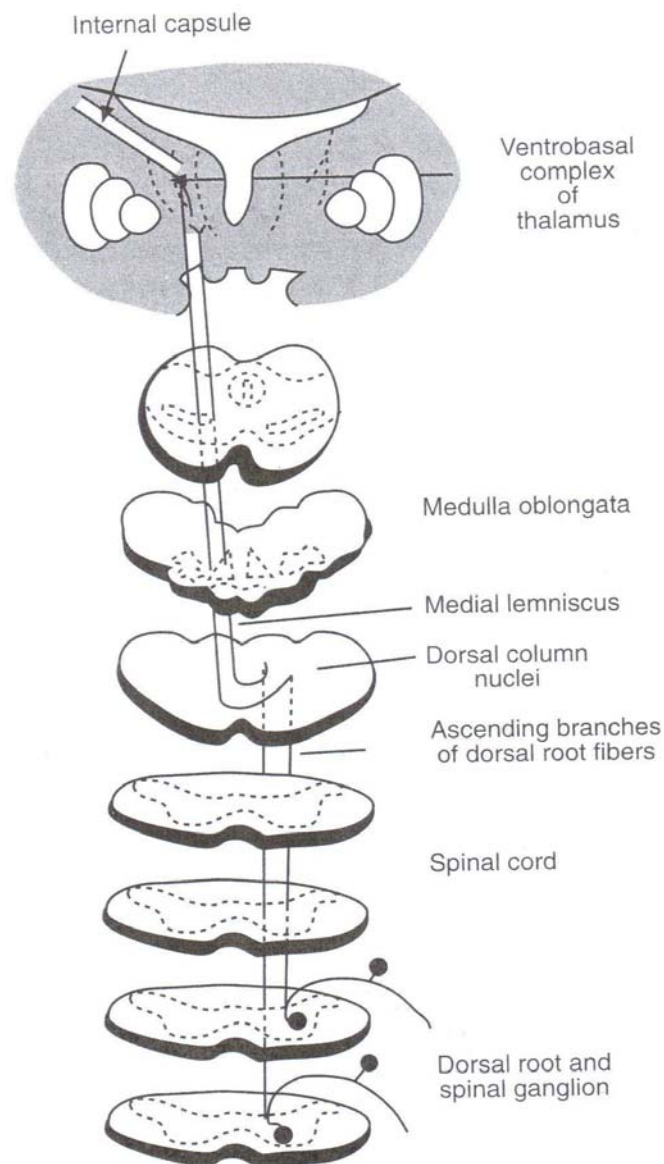
Hair follicle receptors sense light touch and air movements across the skin. Consequently, they are unlikely to contribute to JPS and JK senses.

In conclusion, proprioceptors responsible for joint proprioception are located not only in the joint but in the surrounding muscles, articular capsule and skin. In addition, proprioceptors have different adaptive properties which could be rapid or slow. From the review of literature, it is seems that JK is mediated by rapidly adapting proprioceptors such as the Pacinian corpuscles and lamellated corpuscles (Lephart et al. 1992; Stillman 2002). The slowly adapting proprioceptors such as the Ruffini endings and Golgi tendon organs appear to be responsible for JPS. However, since the some of the receptors are partly slowly adapting and partly rapidly adapting. This suggests that there is an overlap in the proprioceptors responsible for JK and JPS, and these outcomes (JK and JPS) may be affected equally in patients (Stillman 2002).

### **4.3 Central Pathways of Joint Proprioception**

Impulses from mechanoreceptors are conducted to the central nervous system (CNS) via nerve fibres (Barrack and Munn 2000; Gilman 2002; Reimann and Lephart 2002; Snell 2006). The integration of sensory input received from any part of the body is believed to start at the level of the spinal cord (Riemann and Lephart 2002; Snell 2006). The sensory inputs enter the spinal cord predominantly via the dorsal roots (Barrack and Munn 2000) and are divided into medial and lateral divisions. The large diameter ( $\geq 6 \mu\text{m}$ ) medial division fibres serve pressure, discriminating touch, vibration and the other proprioceptive senses. The smaller diameter lateral division fibres serve the senses of pain, temperature, touch and pressure. The posterior column pathway primarily responsible for joint proprioception is illustrated in Figure 4.1.

The main ascending pathways for proprioception in the spinal cord are the fasciculus cuneatus and the spinomedullary tract. They serve the upper and lower limbs, respectively. Fasciculus cuneatus fibres ascend ipsilaterally in the dorsal white column to reach the cuneate nucleus in the medulla. About 15% of these fibres are second order neurones from the nucleus proprius (Rexed laminae IV – VI) in the dorsal grey column. Spinomedullary tract fibres also ascend ipsilaterally but in the posterolateral white column to the Z nucleus in the medulla. All these fibres are second order neurones from the dorsal nucleus in the intermediate grey column.



**Figure 4.1: Posterior column pathway primarily responsible for joint proprioception (Reproduced with permission from Barrack and Munn 2000)**

The fasciculus gracilis, which ascends in the posterior white column adjacent to the fasciculus cuneatus, was originally considered to provide proprioception in the lower limbs. However, the current view is that almost all the proprioceptive information, which initially enters this tract, leaves it again below L2 to enter the spinomedullary tract via a relay through the dorsal nucleus (Barrack and Munn 2000). The fasciculus gracilis almost exclusively transmits the neural substrate for topographically-localised pressure, vibration and discriminative touch sensations derived mainly from the rapidly adapting skin receptors (Schneider 1990).

The second or third order neurones from the cuneate and Z nuclei cross the midline before ascending as the medial lemniscus to the ventroposterior thalamic nucleus. The final order of ascending neurones passes to the sensory regions of the cerebral cortex via the internal capsule. The spinomedullary and cuneate tracts also submit fibres to the cerebellum. The principal ascending pathways for transmission of unconscious proprioceptive and exteroceptive information are the dorsal and ventral spinocerebellar tracts. Second order neurones from the nucleus proprius pass to the dorsal nucleus, which in turn supplies third order neurones ipsilaterally into the dorsal spinocerebellar tract, and contralaterally into the ventral spinocerebellar tract. These spinocerebellar tracts then ascend in the periphery of the posterolateral and anterolateral white matter, respectively. The ventral tract initially crosses the midline before ascending in the opposite side of the spinal cord, these same fibres again cross the midline after entering the cerebellum; hence both spinocerebellar tracts are functionally ipsilateral.

The proprioceptive pathways and their destinations are provided in more detail by Barrack and Munn (2000), Stillman (2000), Riemann and Lephart (2002), Tortora and Grabowski (2003) and Snell (2006).

Peripheral receptors are not the only source of proprioception. During voluntary muscle contractions, there is an accompanying corollary discharge from the corticospinal pathways. The precise site of the corollary discharge pathway is uncertain. During voluntary activities, a replica of the signal from the corticospinal tract to the muscles is transmitted to the sensory regions of the cerebral cortex (Proske et al. 2000). By comparing the corollary discharge with the proprioceptive

afferent feedback from the periphery, the sensory cortex may gain a more specific impression of what is happening peripherally.

Thus, the cortical identification of joint positions during assessment of active JPS may involve interpretation of muscle force, effort and limb segment weight in addition to the information about muscle length and other tissue tensions. Therefore, it appears that the mechanisms for determining JK and JPS when the surrounding muscles are voluntarily or reflexively activated are fundamentally different from those where the muscles are relaxed (Selfe et al 2006).

In conclusion, it is evident that proprioception has different meanings. In this thesis joint proprioception is a combination of JK and JPS. It also seems that the proprioception system involves a complex interaction between peripheral and central neural neuromusculoskeletal mechanisms. Furthermore, sensory receptors that are responsible for JK and JPS are not only located in the joint but other sounding structures such as muscles, tendons and skin.

It seems likely that sensory inputs from the surrounding muscles can be minimised when the muscles involved are relaxed. HMS is associated with ligamentous laxity in conjunction with joint or muscle pain and impaired muscle contraction may be found in individuals with this condition. Therefore, for proprioceptive acuity emanating from the knee joint and the surrounding ligaments to be tested in this study, it was important for the sensory inputs to JK and or JPS from muscles and tendons, visual, and auditory to be minimised. Hence, sensory input into JK or JPS senses from these structures and senses, with the exception of the knee joint structure, of healthy children and those diagnosed with HMS was minimised.

## **4.4 Factors Affecting Joint Proprioception**

### **4.4.1 Background**

The ability of individuals to sense joint position and motion is affected by factors such as age (Barrack et al. 1983b), gender (Rozzi et al. 1999), joint laxity (Blassier et al. 2000), muscle fatigue (Skinner et al. 1986; Gurney et al. 2000) and pain (Baker 2002; Matre et al. 2002). If normative data are to be used to determine whether joint proprioception is impaired in an individual, consideration must be given to these factors. Parts of the aims of the present study are to identify the neuromuscular performance characteristics in children with HMS and the effect of age and gender on these characteristics in healthy children. Therefore, this section discusses the effect of age, gender and joint laxity.

### **4.4.2 Effect of Age**

Studies correlating age with proprioception have found a continuous decline in JK (Barrack et al. 1983b; Skinner et al. 1984) and JPS (Barrack et al. 1983b; Skinner et al. 1984; Barrett et al. 1991) with increasing age. JPS in the articular diseased knee (Barrack et al. 1983b) and normal knee (Hurley et al. 1998) joints have shown a decline in proprioceptive acuity with aging in adults. Due to a paucity of studies specific to children, previous studies that have investigated age-related changes in joint proprioception in both adults and children are summarised in Table 4.3.

**Table 4.3: Summary of studies that have investigated the effect of age on joint proprioception in adults and children**

<b>Authors</b>	<b>Joint tested and population</b>	<b>Method used</b>	<b>Results</b>
Barrack et al. (1983b)	Knee. 11 healthy subjects (mean age 24.9 years) 11 healthy subjects (mean age 63 years)	JK  Passive JPS	The young subjects had significantly better proprioceptive accuracy than the older subjects following both types of assessment ( $p < 0.01$ ).
Skinner et al. (1984)	Knee. 29 healthy subjects (age range 20 – 82 years).	JK and JPS	A significant linear regression between test results and age was obtained following both types of test ( $r^2 = 0.33$ , $p < 0.001$ ).
Crowe et al. (1987)	Index finger. 11 healthy adults (mean age 21.9 yrs), 24 healthy children (mean age 10.3 yrs).	Active fingertip positioning-matching	Children were significantly less accurate than the adults ( $r$ and $p$ values not reported).
Hearn et al. (1989)	Index finger. 134 healthy subjects (age range 8 – 24 years).	Active fingertip positioning-matching	Proprioceptive accuracy increased significantly with age ( $r$ and $p$ values not reported).
Barrett et al. (1991)	Knee. 81 healthy subjects and 45 subjects with OA of the knee and 21 patients who had knee replacement surgery. Ages not reported	Passive JPS	Poorer performance ( $p < 0.01$ , linear regression analysis) observed in older compared with younger subjects.
Ashton-Miller et al. (1992)	Trunk. 253 healthy children (age range 7 – 18 yrs)	Active JPS	Trunk positioning accuracy improved significantly with age ( $p = <0.001$ ).

**Table 4.3 (Continued): Summary of studies that have investigated the effect of age on joint proprioception in adults and children.**

<b>Authors</b>	<b>Joint tested and population</b>	<b>Method used</b>	<b>Results</b>
Petrella et al. (1997)	Knee. 16 subjects with OA of the knee 19 – 27 years, 12 active and 12 inactive subjects 60 – 86 years.	Active weight-bearing tests with active ipsilateral matching responses.	Significantly better JPS was found in the younger subjects than the older ones, and in the active than inactive subjects ( $p < 0.03$ ).
Hurley et al. (1998)	Knee. 45 healthy adults (age range 21 – 82yrs)	Active JPS	JPS was worse ( $p < 0.001$ ) in the elderly subjects than young and middle-aged subjects. JPS acuity decreased as increased ( $r = 0.603$ ; $p < 0.001$ ).
Jerosch (2000)	Shoulder. Elite tennis players (age range 8 – 16 years)	JPS	Subjects older than 12 years had a tendency for better JPS compared to younger subjects.
Goble et al. (2005)	Forearm. 19 children (mean age 9.3 yrs), 9 adolescents (mean age 17.6 yrs)	Passive JPS	Adolescents were significantly better than children ( $p < 0.001$ ).

JK = joint kinaesthesia; JPS = joint position sense; OA = osteoarthritis.

It can be seen that reduced proprioception was found with advancing age in adults. In contrast to the findings on joint proprioception in adults, a significant increase in JPS acuity with increasing age has been reported in children (Crowe et al. 1987; Hearn et al. 1989; Jerosch 2000; Goble et al. 2005). It can be seen from Table 4.3 that the joints examined in adults were different from those investigated in children. Whilst the knee joint has been studied in adults, spinal, forearm and shoulder joints were studied in children. This could have accounted for the contrasting results obtained between children and adults. Moreover, the validity and repeatability of the



testing instruments used for proprioception assessment in children were not reported as a result the observed findings may not represent the overall proprioceptive ability in children.

In summary, it seems likely that joint proprioception decreases with increase in age in adults and increases with increasing age in children. Most researchers investigating age-related changes in joint proprioception have focused on normal adult knees and adults with diseased knees. To date no study was found reporting the pattern of knee proprioception in children. Therefore, to establish a database on the effect of age on knee joint proprioception in children the present investigator examined this phenomenon in healthy children.

#### **4.4.3 Influence of Gender**

The matter of gender-related differences in proprioceptive acuity has mainly been driven by relatively higher rates of knee injuries in female athletes than in their male counterparts. Researchers have hypothesised that reduced proprioceptive acuity is a potential factor predisposing to sports injuries (Rozzi et al. 1999). Better proprioceptive acuity has been reported in men compared with women (Rozzi et al. 1999). At the moment, conclusive evidence has not been reached as regards this issue, as little research has addressed gender-specific patterns of sensation or afferent neural transmission. Accounts of possible gender differences in JK and JPS are discussed below.

Friden et al. (1996) found no differences in knee JK and active JPS between healthy men and women. Similarly, Birmingham et al. (1998) were unable to detect a gender-dependent pattern in JPS. They examined the ability of subjects to actively and passively replicate previously positioned knee joint angles in weight-bearing and nonweight-bearing conditions, with no difference between men and women (Birmingham et al. 1998). Furthermore, Kiefer et al. (1998) observed no gender difference during active knee JPS between men and women ( $p > 0.05$ ).

On the other hand, Rozzi et al. (1999) observed that knee joint kinaesthesia was significantly better in men athletes than the women at a starting position of  $15^{\circ}$  of knee flexion while moving into extension ( $p = 0.039$ ). However, no significant difference was observed in knee joint kinaesthesia while moving into flexion ( $p =$

0.155). It is difficult to draw a definite conclusion from the evidence presented above. Therefore, future studies are required to clarify gender differences in knee joint proprioception in both children and adults.

#### **4.4.4 Joint Laxity and Proprioception**

Unequal distribution of joint loads may cause the articular surface to deteriorate, reduce joint space height and alter the balance of tension on the surrounding soft tissues (Swanik et al. 2000). Deficit in proprioception has been reported in subjects with knee joint laxity (Barrack et al. 1983a) and anterior cruciate deficient knees (Borsa et al. 1997; Beynnon et al. 1999; Robert et al. 2004).

JPS in knees with chronic ACL tears has been demonstrated to be impaired when compared to the contralateral uninjured knee (Barrett 1991; Corrigan et al. 1992). Altered knee joint kinaesthesia was also demonstrated in subjects with chronic ACL tears (Corrigan et al. 1992). Additionally, a significant deficit in angular reproduction at the proximal interphalangeal joint (Mallik et al. 1995) and knee JK (Hall et al. 1995) was demonstrated in patients with HMS compared to aged-matched controls. A summary of studies that examined the effect of joint laxity on proprioception is illustrated in Table 4.4.

All the authors except for Stillman et al. (2002) demonstrated impairment in joint proprioception in subjects with joint laxity compared with controls.

The reason for the opposing results by Stillman et al. (2002) may be that active JPS was examined in their study.

**Table 4.4: Summary of Studies Investigating the Effect of Joint Laxity on Proprioception**

<b>Authors</b>	<b>Joint tested and population</b>	<b>Method(s) used</b>	<b>Results</b>
Barrack et al. (1983a)	Knee. 12 ballet dancers (mean age 25 yrs), 12 healthy controls (mean age 24 yrs)	Passive JPS	Ballet dancers with GJL were significantly worse than controls in their ability to reproduce angles ( $p = 0.03$ )
Corrigan et al. (1992)	Knee. 37 subjects (20 subjects with torn ACL, mean age = 30 yrs; 17 healthy controls, mean age = 28 yrs).	JK Active JPS	Diminished JPS and JK in the injured ACL deficient knees compared with the control group ( $p$ values not reported).
Blassier et al. (1994)	Shoulder. 29 healthy subjects (age range 20 - 40 yrs)	JK	Subjects with joint laxity had significantly worse JK than those without joint laxity ( $p < 0.002$ )
Mallik et al. (1994)	Proximal interphalangeal joint. 12 women with HMS (mean age 29 yrs) , 12 healthy women (mean age 29 yrs)	Passive JPS	HMS patients were significantly less accurate than the control group ( $p < 0.0001$ )
Hall et al. (1995)	Knee. 10 women with HMS (mean age 30 yrs)	JK	JK was significantly worse in HMS patients than the control ( $p < 0.001$ at both angles starting angles of 5 and 30 degrees)
MacDonald et al. (1996)	Knee. 8 subjects, 10 patients with PCL deficient knees (mean age 34 yrs),	JK	JK was statistically better in contralateral control knees than the PCL deficient knees ( $p = 0.0286$ )

**Table 4.4 (Continued): Summary of Studies Investigating the Effect of Joint Laxity on Proprioception**

<b>Authors</b>	<b>Joint tested and population</b>	<b>Method(s) used</b>	<b>Results</b>
Borsa et al. (1997)	Knee. 29 ACL deficient athletes (mean age 28.7 yrs)	JK	Deficit in threshold to detection was statistically significant for ACL deficient knee compared with control at 15 degrees (p = 0.01)
Beynnon et al. (1999)	Knees. 20 patients with ACL deficient knees (mean age 40 yrs)	JK	Threshold to detection was worse in patients with chronic ACL insufficiency compared with uninjured knees (P = 0.011)
Stillman et al. (2002)	Knee. 44 active healthy subjects (mean age 21.1 yrs)	Active JPS	JPS was statistically better in subjects with greater knee mobility than those with less knee mobility (AAE p= 0.03, AEV p = 0.03). No significant difference between RAE (p = 0.93).
Roberts et al. (2004)	Knee. 54 patients with ACL deficient knees (mean age 28 yrs)	JK	Statistically higher threshold to detection values was found with increased joint laxity (p = 0.04)

JPS = joint position sense; JK = joint kinaesthesia; AAE = absolute angular error; AEV = angular error of variation; RAE = relative angular error; ACL = anterior cruciate ligament; GJL = generalised joint laxity

Active JPS testing involves both motor and sensory receptors (Barrett et al. 1991), therefore, proprioceptive contribution from muscles acting on the knee joint could have influenced the findings. Additionally, the participants in the study by Stillman et al. (2002) had a history of regular sport spanning more than 5 years. It was not

stated if participants with greater knee mobility engaged in sports more than those with less knee mobility. It has been reported that proprioception is enhanced by exercise training (Petrella et al. 1997; Ashton-Miller et al. 2001; Roberts et al. 2004). Therefore, it is unknown whether the better proprioceptive acuity found in participants with greater knee mobility was as a result of the level of activity.

This section has demonstrated that impaired joint proprioception may be associated with joint laxity. It is also clear that joint proprioception has been studied in adults with both joint laxity and HMS. The findings of these investigations (Table 4.4) may not however be transferable to children with joint laxity and HMS. Therefore, further work is required to clarify this issue.

In summary, age and gender-related changes in joint proprioception have been investigated in adult populations and children. It seems that proprioception decreases with increase in age in adults. On the other hand, it appears that proprioceptive acuity increases with increasing age in children. However, opinions differ as to the influence of gender on JPS and JK. Moreover, proprioceptive impairment appears to be associated with joint laxity and HMS in adults. The present research therefore investigated the effect of age and gender on JK and JPS. It also identified the possible effect of HMS on JK and JPS.

In the next section, the methods used for clinical assessment of joint proprioception are discussed.

## **4.5 Clinical Assessment of Joint Proprioception**

Joint proprioception has been assessed using various methods. At the moment, there are no standardised methods of assessing proprioception. Therefore, this section describes the various methods previously used for assessing joint proprioception. It also examines the strengths and weaknesses of the methods. More detailed account of methods of proprioception assessment is provided by Stillman (2000).

### **(a) Visual Estimation**

A common clinical method of JPS assessment involves the examiner passively holding a joint in a chosen test position whilst the patient with eyes closed attempts to match this position using the same joint in the opposite limb (Adams and Victor 1993; Marks 1998). The examiner then observes the degree and direction of any mismatch between the two joint positions. The method of scoring these responses is not generally stated in the literature. Usually, each of several responses is assessed using a simple categorical scale such as in the study of Lincoln et al. (1998). Even normal subjects rarely produce perfect matches hence, clinicians may find it difficult to estimate whether a given mismatch is normal or abnormal in children with HMS.

Passive JPS tests with contralateral limb matching were investigated in a group of stroke patients using visual estimation (Lincoln et al. 1998). In that study, the patients' responses were subjectively assessed by several examiners using four grades; 'no appreciation of movement of the examined joint', 'appreciation of movement but not its direction, appreciation of the direction of movement', and 'placement of the responding limb within 10° of the test position'. A poor inter-rater repeatability (Cohen's kappa = 0.49) of this scale for JPS test was reported.

Similarly Sartor-Glittenberg and Powers (1993) examined elbow JPS in stroke patients where the contralateral matching responses were graded as 'normal', 'slightly disturbed' or 'severely disturbed'. Their findings were compared with the results from an independent examiner who used a sophisticated psychophysical assessment of pairs of marginally different elbow flexion angles. The sets of their results were significantly different ( $p = 0.001$ ). The psychophysical methods of assessment used are described below in section 4.6.2.

In contralateral limb matching responses, it may be difficult for clinicians to visually estimate the joint positions in angular degrees. This view is supported by the studies on visual estimation of angular positions of the knee (Watkins et al. 1991) that produced poor intra- and inter-rater repeatability.

According to Stillman (2000), there are two other clinical assessment procedures with features similar to tests with contralateral limb matching responses. First is the active assessment where the subject with eyes closed simultaneously flexes both elbows joints to a self-selected position, after which they estimate the mismatch between the two joints (De Domenico and McCloskey 1987). Secondly, the JK test described by Sims et al. (1996) where the subject with eyes closed grasped a handle on each of two wooden ramps with independently controllable slopes between 0 and 20°. With the slope of the two ramps different by increasing amounts in increments of 3 – 5°, the examiner slides the handles to the top of each ramp then asked the subject to say which hand is higher.

Because both limbs are simultaneously involved in tests with contralateral limb matching responses, when the contralateral joint is proprioceptively impaired, it may be difficult for an examiner to isolate the individual contributions from each joint to the obtained result. Examples are in stroke, where the non-affected limbs may also be proprioceptively impaired (Sartor-Glittenberg and Powers 1993), and in diabetic neuropathy, which is not always symmetrical but bilateral (Horowitz 1993). Additionally, using contralateral matching may not be appropriate in clinical settings as there may not always be a contralateral joint available for examination, for instance where one limb of a child has been immobilised.

#### **(b) Non Visual Location**

The non-visual location of the extremities of body segments in space is another method of JPS tests (Stillman 2000). Shoulder JPS was tested by having subjects touching an object in front of the body with an outstretched finger (Forwell and Carnahan 1996). Another category of JPS test is the thumb finding test. In this test, the examiner passively positions one upper limb with the patient's eyes closed and then asks the patient to touch the thumb of the positioned limb with the opposite hand (Hirayama et al. 1999). Finger-to-nose and finger-to-finger tests are other forms of such tests (Keessen et al. 1992).

It has been shown that tests involving the spatial location of finger tips produce different results compared to assessing the location of finger joint positions (Biggs and Horch 1999). Therefore, it is possible that these two tests have different central neural processing pathways. Tests involving the location of finger tips in space may have as much functional relevance as active JPS tests of the lower limb (Stillman 2000). Presently the results of these tests are not quantified.

Subjective tests have limited repeatability. Leo and Soderberg (1981) examined the thumb-finding capacity of stroke patients and reported good interrater repeatability (ICC = 0.54). They used three subjective grades — inability to find the thumb, movement of the opposite hand in the general direction of the thumb, and direct location of the thumb. It is believed that abnormal results may also be caused by non-proprioceptive disorders, particularly of the cerebellum (Stillman 2000).

### **(c) The Romberg Test**

Proprioception of lower limb joints, especially the ankles has been assessed using some form of the Romberg test (Ryan 1994). This test involves evaluation of posture and sway with the subject standing on one or both feet on a stable or unstable base with eyes open then closed (Hoffmann and Payne 1995). It is believed that standing on an unstable base may challenge balance mechanisms (Stillman 2000).

The proprioceptors in all joints throughout the weight bearing lower limb(s) may be affected. Consequently, increased sway in standing may not necessarily represent poor performance of proprioceptors in the examined joint as other structures such as muscles will also be involved during standing. Bernier and Perrin (1998) demonstrated this in the study of unstable ankles. They discovered that standing balance was improved following a six-week programme of balance and coordination exercises but there was no change in the results following tests of ankle JPS. It is difficult to isolate other weight bearing joints such as the ankle and hip when using the Romberg test to test the knee joint in children with HMS.

In conclusion, many of the assessment methods presently used for testing proprioception are not very repeatable, may limit the ability to determine and quantify abnormality. Therefore, they may not be suitable for assessing children with HMS.



#### **4.5.2 Other Tests of Proprioception**

Proprioception also consists of estimation of weights, forces and effort (Stillman 2000). The ability with eyes closed to differentiate marginally different weights held in the hand, to estimate the compliance of a spring compressed between a finger and thumb, to judge the effort associated with resisted voluntary muscle contractions, and to sense the vibration of a tuning fork applied to a bony prominence, are all valid tests of proprioception (Stillman 2000). There is little evidence of any clear correlation between the results from such assessments. This suggests that each of the methods of assessment may be assessing different components of proprioception.

Cox (1991) found a poor correlation between the ability of healthy subjects to distinguish between weights held in the hand and forearm pronation-supination JPS. It has been demonstrated that joint proprioception, vibration sense and skin discriminatory senses may be affected separately or in various combinations in patients with parietal stroke (Bassetti et al. 1993). Simoneau et al. (1992) found a poor correlation ( $r^2 < 0.34$ ) between ankle plantar/dorsi-flexion JPS tests in diabetic patients.

In a study by MacLennan et al. (1980), a poor correlation between hallux position sense and vibration sense about the wrist and ankles was found in healthy subjects aged at least 65 years. Similarly, Lanska and Kryscio (2000) observed a poor correlation between the results of the thumb finding test, JPS and vibration tests. On the other hand, Moberg (1990) demonstrated a correlation between two-point discrimination and finger JPS. Going by these findings, researchers have suggested that clinicians should not consider substituting one assessment of proprioception for assessment of JK and or JPS (Stillman 2000) as one test may be assessing different component and may not represent the overall proprioceptive ability (Grob et al 2002).

## **4.6 Methods of Assessing Joint Proprioception in Clinical Research**

In clinical research, joint proprioception assessment is characterised by the use of measuring instruments or complex subjective psychophysical methods (Stillman 2000). These research procedures and their possible use for assessment are examined below. Detailed account of methods of joint proprioception assessment in clinical research is provided by Stillman (2000).

### **4.6.1 Psychophysical Sensory Testing**

Psychophysical sensory testing is commonly used by clinical psychologists to assess the ability of subjects to perceive the magnitude of applied sensory stimuli (Stillman 2000). These stimuli include loudness, brightness and pain or the difference in magnitude between marginally dissimilar stimuli (Stillman 2000). This is usually tested by having the subjects respond to each stimulus or a pair of stimuli using simple verbal responses (Coren et al. 1994). JPS has been assessed using these procedures. Jones (1976) tested the ability of children to detect a constant velocity 5° passive elbow movement. This author repeated the test movement 50 times, randomly combined with 50 occasions where no movement was produced. After each test the children were asked to indicate whether or not they sensed movement by responding yes or no. Signal detection theory (Weiler and Awiszus 1997) and the staircase method of adaptive testing (Waddington and Adams 1999) have been used for testing JPS.

Magnitude of estimation is another form of psychophysical assessment. It was used in JPS research by DeBacher (1989). The researchers assigned a rating scale with a convenient range of numbers to a selected range of joint movement. DeBacher (1989) assigned 0 – 100 to the total available range of wrist flexion-extension. Thus, if the available range of wrist flexion-extension was 50°, each unit of the rating scale would represent 2° of wrist movement. Wrist JPS was then assessed in two ways. In the first method the examiner specified a number from the scale after that. The patients (with eyes closed) then attempted to actively move the joint to the equivalent position. In the second method the examiner passively placed the wrist in a specific position with the patients' eyes closed and then they were asked to describe the position using an equivalent number from the scale.

Stillman (2000) believed that the psychophysical assessments described above have the following limitations. First, many repetitions are required in order to properly evaluate patients' proprioceptive acuity. Secondly, a high level of cooperation is required from each patient. Children, and researchers, are likely to find this type of assessment both time-consuming and taxing on their powers of concentration. Therefore, in children, this number of test repetitions would be unrealistic.

Moreover, it is uncertain whether joint proprioception is normally perceived in numerical terms by individuals (Stillman 2000). Therefore, magnitude of estimation tests, which focus on the numerical equivalent of proprioception, may not produce representative results of each individual's true proprioceptive ability.

#### **4.6.2 Arthrokinetic Reflexes**

Assessment of this proprioceptive function involves stressing or suddenly moving the joint then recording any reflex reaction in the surrounding muscles (Jennings and Seedham 1994; Beard et al. 199; Beard et al. 2000). This method of assessment requires special equipment to generate the stresses and record the muscular responses. This test may be unsuitable for children with HMS as impaired muscle reflexes (Ferrell et al. 2007) and muscle weakness (Sahin et al. 2007) have been found in individuals with HMS.

Additionally, this type of assessment cannot be easily administered and it is likely that the results from JPS tests and arthrokinetic reflexes will vary since the neural pathways involved in proprioceptive sensation and protective articular reflexes are different (Stillman 2000). However, the relationship between JPS and JK and arthrokinetic reflex tests is yet to be reported.

#### **4.6.3 Visually-Oriented Methods**

Assessment of JPS in clinical research includes asking the subject to reposition a joint incorporating a protractor scale (Warren et al. 1993; Attfield et al. 1996; Friden et al. 1996). It also consists of positioning a pointer over a protractor scale (Carey et al. 1996). Subjects may sometimes be asked to manipulate a line diagram of the joint displayed on a computer screen (Rodier et al. 1991; Euzet and Gahéry 1995). The use of vision with the use of peripheral proprioceptors to identify limb positions

may indicate fundamental differences between the neural methods used to process these two types of information (Soechting et al. 1996; van Beers et al. 1999). Visual processing of proprioceptive information has been reported to be less accurate and less repeatable than tests with limb matching responses (Friden et al. 1996). Therefore, visually oriented tests may not be suitable for proprioception assessment in children with HMS.

#### **4.6.4 Joint Kinaesthesia Tests**

Joint kinaesthesia tests or threshold to perception of low velocity passive movement are common in clinical research (Hall et al. 1995; MacDonald et al. 1996; Borsa et al. 1997; Beynnon et al. 1999; Ferrell et al. 2004; Roberts et al. 2004). With the subject's eyes closed or blindfolded, the joint is passively moved from the chosen starting position at a low velocity of  $0.4^{\circ}/s$  to  $0.5^{\circ}/s$  (Friden et al. 1997; Rozzi et al. 1999; Ferrell et al. 2004; Roberts et al. 2004; XU et al. 2004; Ageberg et al. 2005; Ageberg et al. 2007). The subject is asked to indicate when a change in joint position is perceived, along with the direction of change.

The amplitude of movement indicated by the subject can then be measured trigonometrically. For instance, the knee angle of flexion is calculated as the arctangent of the distance moved by the lateral malleolus divided by the length of the leg. This method requires a customised motorised apparatus to produce the low velocity passive movements. It has been used for assessing the knee (Barrack et al. 1983c; Lephart et al. 1992; Hall et al. 1995; Ferrell et al. 2004).

Additionally, each subject is usually required to listen to white noise or music through headphones to block out noise from the motor (Friden et al. 1997; Ageberg et al. 2005; Ageberg et al. 2007). An air splint may also be placed around the proximal and distal joint segments to minimise extraneous proprioceptive input from the skin (Hall et al. 1994; Ferrell et al. 2004). These precautions are inconvenient, time consuming and impractical for routine clinical assessments. Moreover, the use of headphones with white noise may distract children during testing (Taylor et al. 1998). Therefore, air splints and headphones were not used in the present study.

#### **4.6.5 Angular Reproduction Tests**

Proprioception has been assessed in some clinical studies by measuring an individual's ability to actively (Stillman et al. 2002; Bennell et al. 2003; Bennell et al. 2005) or passively (Tsang and Hui-Chan 2003; 2004; Selfe et al. 2006) reproduce test positions. Joint position sense (JPS) or matching response can be performed either by using the same joint in the opposite limb (test with contralateral matching response) (Remedios et al. 1998) or the examined joint (ipsilateral matching) (Bennell et al. 2003; Bennell 2005; Selfe et al. 2006). This is usually done with the subject's eyes closed or blindfolded. In both procedures the examiner usually passively supports the examined joint in each test position, but actively maintained test positions have also been used (Ishii et al. 1997; Good et al. 1999).

The clinical relevance of passive tests for assessment of JPS has been previously challenged (Stillman 2000; Baker et al. 2002). Such challenges are based on the argument that active tests produce more accurate and repeatable results, and that the proprioceptive system is normally required to function under circumstances where the muscles are voluntarily or reflexly contracted (Gandevia et al. 1992; Kalaska 1994; Petrella et al. 1997; Marks 1998; Good et al. 1999; Stillman 2000; Baker et al. 2002).

Gandevia et al. (1992) believed that the sensations of positions and movements of joints are rarely generated in the absence of muscular contraction. Furthermore, the sensation of joint rotation is routinely not assessed clinically when joints are moved passively. Kalaska (1994) was of the opinion that somesthesia is not a strictly passive process and that peripheral proprioceptive signals are altered by active muscle contractions.

It has been suggested that active JPS involves different and possibly more natural central nervous processes than passive tests (Stillman 2000). In addition, it is believed that greater level of peripheral afferent information is generated during active JPS compared to passive JPS (Selfe et al. 2006). There is this issue of whether active tests can be administered by clinicians in a more repeatable manner than passive tests. Moreover, subjects' relaxation during passive tests may be difficult to achieve (Beynnon et al. 2000). Some passive tests may involve unintended muscle contractions, which may be unrecognised by the examiner.

Similarly, there may be input from proprioceptive receptors emanating from contracting muscles during active tests. Therefore, active tests and 'true passive' tests may produce different results, and may lead to inappropriate interpretation of results. Acknowledging these limitations in the use of passive tests, they could be used effectively for assessing JPS in children who may be unwilling to perform an active JPS test. Moreover, a passive JPS test may be a useful technique for assessing proprioceptive ability of patients with associated muscle weakness due to pathological problems. Hence, a passive test was used for JK and JPS assessment in the present study.

#### **4.7 Instruments Used for Assessing Proprioception**

Proprioception has been measured using purpose-built apparatus incorporating a simple protractor scale (Barrett 1991); hinged protractor goniometer (Kaplan et al. 1985); electrogoniometers (Petrella et al. 1997; Kiefer et al. 1998; Kramer et al. 2001); dynamometer (Callaghan et al. 2002; Sekir and Gur 2005; Selfe et al. 2006); dynamometers incorporating an electrogoniometer (Kiefer et al. 1998; Remedios et al. 1998; Tsang and Hui-Chan 2003; 2004); and purpose-built motorised devices (Barrack et al. 1983a; Barrack et al. 1983b; Hall et al. 1994; Grob et al. 2002; Ferrell et al. 2004; Ageberg et al. 2005; 2007). In this section, instrumented methods of assessing joint proprioception are discussed. Motorised devices are discussed in the following chapter.

##### **(a) Simple Protractor Goniometry**

Simple protractor goniometry could be problematic during JPS tests with contralateral matching responses. This is because valid comparisons of measurements from contralateral joint depend on the goniometers being related to each joint in exactly the same way (Stillman 2000). This problem has been demonstrated in the study of knee JPS by Remedios et al. (1998) and is an unnecessary burden to be imposed on clinicians and researchers during the assessment of patients. The use of a hinged protractor goniometer may also introduce errors of repeatability as it may be difficult to standardise the goniometer placement during measurements.

**(b) Electrogoniometers**

Electrogoniometers have been used for assessing knee joint proprioception in healthy adults (Petrella et al. 1997; Kramer et al. 2001). It is believed that electrogoniometers are more sophisticated than a hinged protractor goniometer (Isacson et al. 1986). The accuracy and repeatability of electrogoniometers may be affected by how well it is initially related to bony landmarks and the extent of its movement over the skin when in use. Kerrigan et al. (1998) recognised that electrogoniometers have a relatively poor accuracy because they were very difficult to apply. Moreover, there may be problems due to poor calibration. In a study of knee JPS by Kiefer et al. (1998) the electrogoniometer were calibrated against four angles on a protractor goniometer, thus transferring any inaccuracies in the protractor goniometer or its operator to the electrogoniometer.

**(c) Dynamometers**

Dynamometers are valid tools for measuring muscle torque (Wiggin et al. 2006). They have also been used for assessing knee joint proprioception in healthy adults (Hurley et al. 1998; Callaghan et al. 2002; Tsang and Hui-Chan 2004) and adults with pathological conditions (Sekir and Gur 2005). However, their use is impractical for clinical assessment of proprioception in children as the lever arm of dynamometers may be too big, making it difficult to correctly align the knee axis with the centre of rotation. Dynamometers are expensive (Wiggin et al. 2006) and may therefore not be available for routine clinical use. As a result, their use for knee joint proprioception assessment in children is limited and were not used for knee joint proprioception assessment in this research.

**(d) Video- and Photograph-based Goniometry**

Video- and photograph-based goniometry is usually used by placing reference markers over surface landmarks so as to outline the joint angles to be measured. Sophisticated computer-based video measurement systems have been used in previous studies of JPS (Darling 1991; Feuerbach et al. 1994; Forwell and Carnahan 1996; Brumagne et al. 1999; Lonn et al. 2000). Knee JPS has also been examined using photography (Marks 1996; Marks and Quinney 1997) and/or video-recording (Stillman et al. 2001; Baker et al. 2003; Bennell et al. 2005). Computer-based video measurement systems are very complex, expensive, time-consuming and not generally available for clinical use. Video methods may not be repeatable

because of marker placement as they may be associated with significant skin movement. Moreover, regarding photography method, the film is expensive and processing the photographs may be time-consuming. Therefore, it is clinically inconvenient for proprioception testing in children.

In summary, the basis of any clinical assessment is to know whether there is an abnormality, identify its type and location, determine its severity, and/or examine its progress. Clinical assessment of proprioception should be simple, safe, time efficient, as well as being valid, accurate, repeatable and sensitive to small changes. Active tests may be more accurate, repeatable and be of greater functional and clinical relevance than passive tests. However, they may not be appropriate in children and certain groups of patients such as those with pathological problems. Instrumented measurements may be necessary to obtain accurate, repeatable and sensitive results.

Based on this review of literature it appears that passive JK and JPS tests using purpose-built apparatus such as motorised devices both have their limitations. However, they are still the most commonly used method in clinical and research studies. Issues related to purpose-built motorised devices for joint proprioception assessment are examined in the next chapter.

#### **4.8 Relationship between JK and JPS**

Many authors believe that JK and JPS are components of joint proprioception (Table 4.1). Knee joint proprioception has been previously tested using JK (Hall et al. 1994; Ferrell et al. 2004), JPS (Fremerey et al. 2000; Tsang and Hui-Chan 2004) or both tests (Barrack et al. 1983b; Barrett et al. 1991; Sekir and Hakan 2005). Results of proprioceptive tests may differ depending on the test used.

Skinner et al. (1984) found a weak ( $r = 0.293$ ) but significant ( $p < 0.025$ ) relationship between knee JK and JPS measures in 29 healthy subjects (students and hospital staff) aged 22 to 82 years indicating that the similar biological parameters might have been assessed by both tests. In a study of effect of fatigue on knee joint proprioception by Skinner et al. (1986) using a motorised device, a high correlation ( $r = 0.759$ ,  $p = 0.01$ ) between JK and JPS was reported before fatigue. A low correlation ( $r = 0.5$ ,  $p = 0.118$ ) was found after fatigue. 11 healthy male volunteers



(aged 19 to 28 years) from the US Navy who had completed the final and most rigorous phase of training were studied.

Although Skinner et al. (1984) and Skinner et al. (1986) used similar method and testing devices, the subject characteristics used in the two studies were not the same. For instance, the level of activity and age range of the participants were different. Additionally, JK was tested by Skinner et al. (1984) using an angular velocity of  $0.4^{\circ}/s$  while Skinner et al. (1986) used an angular velocity of  $0.5^{\circ}/s$ . Moreover, the pressure of the custom-made air splints used by Skinner et al. (1984) to minimise cutaneous input was 20 mm Hg, while Skinner et al. (1986) used custom-made air splints inflated to 25 – 30 mm Hg in their study. These methodological differences could have accounted for the conflicting findings.

In a recent study the correlation between different measurements of proprioception (JK and JPS) of the knee joint was investigated in 30 healthy subjects (24 to 72 years) by Grob et al. (2002), using a motorised device. No correlation was found between knee JK and JPS tests (Spearman (r) range -0.25 – 0.33). The results of the above studies suggest that each test may assess different facets of proprioception and that different proprioceptors may be responsible for each of them. For instance, the rapidly adapting proprioceptors are believed to mediate JK while JPS is sensed by the slowly adapting ones (Lephart et al. 1992; Stillman 2002). The details of these proprioceptors have previously been presented in section 4.3.2.

The few studies reported above were conducted in healthy adults and their findings may not therefore transferable to children. It is believed that there is substantial overlap in the receptors mediating JK and JPS and both could be impaired by joint injury or disease (Stillman 2002). Based on this assumption and the conflicting results on the correlation between JK and JPS, both methods were used for assessing proprioception in the current project. To determine the appropriateness of these measures of proprioception, it was necessary that the relationship between them be investigated in healthy children. As a result, the correlation between knee JK and JPS tests were examined.

## 4.9 Joint Position Sense Measurement Errors

Differences exist in terms of measurement errors used for data analysis of JPS assessment. Three types of errors have been used by investigators for JPS test measurements. These are the absolute angular error (AAE) (Skinner et al. 1984; Barrett et al. 1991; Gottlieb et al. 1994; Ludon 2000; Tsang and Hui-Chan 2004), relative angular error (RAE) (Baker et al. 2002; Stillman et al. 2002) and angular error of variation (AEV) (Feuerbach et al. 1994; Beynnon et al. 2000). Each of these errors represents a unique way of describing JPS. The summary of studies using various types of errors is provided in Table 4.5. Illustration of joint position sense measurement errors (test angle of  $25^{\circ}$  knee flexion) is provided in Figure 4.2. This section describes these measurement errors.

### Absolute Angular Error (AAE)

AAE is the absolute difference between the test and perceived angles. AAE contains only the magnitude information. AAE cannot be used to determine if a subject underestimates or overestimates the target or test positions. Therefore, it represents the subjects overall ability to reproduce the test angle.

### Relative Angular Error

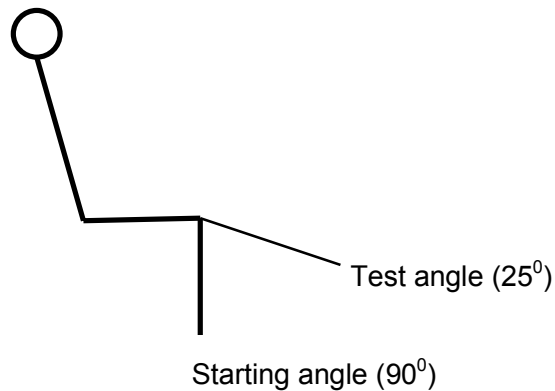
Relative angular error (RAE) is the signed arithmetic difference between a test and perceived angle. The terms 'relative angular error' (Bennell et al. 2003; Bennell et al. 2005) and 'constant error' (Goodman and Marks 1998) have been used interchangeably. To avoid confusion in the use of these terms, the term relative angular error (RAE) is used throughout this thesis. The average RAE is a measure of bias that is the tendency to under-estimate or over-estimate. It contains both the magnitude and direction of information. It characterises how a subject systematically over-estimates or under-estimates the test angle. RAE depends on the relationship between the starting position, test angle and response angle. Under-estimation is usually represented with a negative value (for instance the RAE in example 1 of Figure 4.2 =  $-10^{\circ}$ ) while over-estimation is represented with a positive value (the RAE in example 2 =  $+10^{\circ}$ ).

**Table 4.5: Summary of Studies using Different Errors for JPS Calculation**

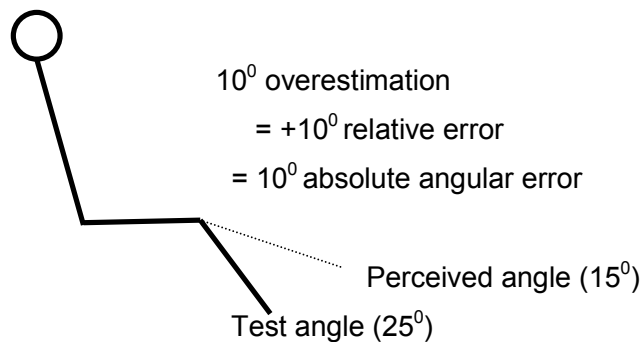
Author	Population/age	Joint Tested	Technique	Error (s) used	Remarks
Hurley et al. (1998)	45 healthy adults (age range 21 – 82yrs)	Knee	Active	AAE	Repeatability not reported
Beynnon et al. (2000)	30 healthy subjects (age range 18 – 34yrs)	Knee	Active Passive	AAE, RAE, AEV	Visual analogue used for angular measurement
Ludon (2000)	24 healthy (mean age 24yrs)	Knee	Active	AAE	Dynamometer and Electrogoniometer used
Stillman et al. (2001)	20 healthy subjects (mean age 19.9yrs)	Knee	Active Passive	AAE, RAE, AEV	-
Bennell et al. (2003)	220 patients with OA of the knee (mean age 68.6 yrs)	Knee	Active	AAE, RAE, AEV	Excellent test-retest repeatability of AAE, RAE (ICC = 0.86 to 0.94). Poor test-retest repeatability of AEV (ICC = 0.44)
Tsang and Hui-Chan (2003)	35 healthy adults (60 yrs and older)	Knee	Passive	AAE	Dynamometer and Electrogoniometer
Bennell et al. (2005)	17 healthy adults (age range 21 – 82)	Knee	Active	AAE, RAE, AEV	JPS assessed using video recording of knee angle, formula used for angular displacement calculation not reported

AAE = absolute angular error; RAE = relative angular error; AEV = angular error of variation; ICC = intraclass correlation coefficient; OA = osteoarthritis

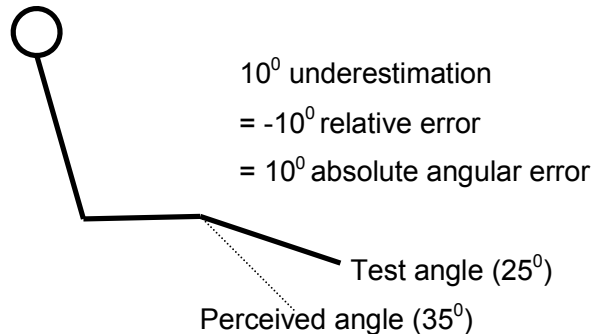
### JPS Test at $25^{\circ}$



#### Example 1: Overestimation



#### Example 2: Underestimation



**Figure 4.2: Illustration of Joint Position Sense Measurement Errors (test angle of  $25^{\circ}$  knee flexion)**

Starting angle = the angle from which the knee joint is moved to the test and perceived angles; test angle = angle that examiner place subjects' knees in which they are asked to sense; perceived angle = angle which the subjects place their knee and they believe it corresponds to test angle.

Using RAE, it may not be possible to say that a group has better or worse proprioception than the other, even if the mean values are significantly different. This can happen if a group has a mean greater than zero and the other cohort achieves a mean of similar magnitude but negative (Stillman 2000). Additionally, RAE may fail to find differences that exist when AAE are used (Beynnon et al. 2000).

### **Angular Error of Variation (AEV)**

The angular error of variation (AEV) represents the precision of a subject's estimate of the test angle. It is the repeatability of responses of a subject following a set of repeated trials. It is commonly described by the standard deviation from the mean of the relative angular errors. Using AEV may lead to difficulties in analysis and interpretation since individuals with lower values are said to be having poorer JPS. There are several potential difficulties with the use of AEV. First, AEV will be increased by random errors in measurement of JPS. Secondly, subjects would be classified as having excellent joint proprioception if they constantly err to any degree, as long as the errors are consistent. Moreover, AEV may ignore learning effects that may be associated with repeated JPS tests.

AAE has been used exclusively for JPS analysis (Birmingham et al. 2000; Ludon 2000). The reason for this may be due to the relative simplicity of interpretation and the possibility that RAE is not sensitive to differences in JPS. Feuerbach et al. (1994) used both AAE and RAE for their data analysis. Significant differences were observed when analysing the AAE but no differences when analysing the RAE. Additionally, Beynnon et al. (2000) reported that AAE was more accurate and repeatable than the RAE and AEV. On the other hand Bennell et al. (2003) found that both AAE and RAE were more repeatable (test-retest, ICC = 0.86 to 0.94) than AEV (ICC = 0.44).

From the foregoing, it seems likely that AAE method of data analysis is accurate, repeatable, can easily be calculated and interpreted. Moreover, AAE has been commonly used and therefore, it was used for JPS tests calculations in this thesis.

#### **4.10 Overall Summary**

In conclusion, subjective assessment methods of assessing joint proprioception may be associated with poor repeatability, bias and difficulty quantifying. This might limit the ability of clinicians to determine and define the level of proprioceptive impairments. Additionally, quantifiable testing methods of assessing proprioception such as magnitude of estimate are time consuming. Moreover, the photographic methods are expensive and require high level of personnel training.

Active JPS, as opposed to passive JPS tests may be functionally and clinically relevant. However, sensory inputs from muscles acting on the test joint are difficult to isolate when active JPS tests are administered. In addition, active JPS tests in pathological conditions such as HMS that is associated with muscle reflex dysfunctions (Ferrell et al. 2007) and muscle weakness (Sahin et al. 2007) may be difficult to examine. Because of these reasons a quantifiable measure of proprioception using passive test and a purpose built motorised device was used in the present study.

The following chapter explores the use of a purpose-built motorised device for assessing joint proprioception in children.

## **CHAPTER 5 : EQUIPMENT DEVELOPMENT AND VALIDATION**

### **5.1 Introduction**

From the previous chapter it is clear that many methods used to assess joint proprioception may not be appropriate in children as they may be time consuming. While active JPS tests have been used previously, it may be difficult to isolate motor contribution to proprioception (Tsang and Hui-Chan 2003; Tsang and Hui-Chan 2004) which may be impaired in individuals with disorders such as HMS. These considerations therefore led to the development of a purpose-built motorised device to assess joint proprioception in this study. Chapter 5 explores the literature relating to the use of motorised devices for assessing joint proprioception and gives a detailed account of the development of a purpose-built motorised device for assessing knee joint proprioception in this study. Issues related to calibration, accuracy and validity of the measurement tools used in the current study are also explored.

#### **5.1.1 Motorised Device for Assessing Joint Proprioception**

A motorised device was first developed and used by Barrack et al. (1983a, 1983b). It consisted of a slow-speed motor mounted on a shaft and a motor control with a patient's on/off switch. Such motorised devices produce constant passive angular displacement of the knee joint (Grob et al. 2002). It is believed that a slow and constant angular velocity maximally stimulate joint proprioceptors (Barrack et al. 1989; Friden et al. 1996; Ageberg et al. 2005; 2007) and minimises the contribution from muscle receptors (Ageberg et al. 2005; 2007) by limiting reflexive muscle contraction (Callaghan et al. 2002). In addition, a slow speed motorised system ensures that subjects will not be able to easily detect the onset of joint motion (Friden et al. 1996).

#### **5.1.2 Advantages of Motorised Devices**

Motorised devices have the following advantages over other methods of joint proprioception assessment. In comparison with visual estimation, they provide quantifiable information regarding the proprioceptive ability of individuals. Motorised devices are easier to use compared with dynamometers and video or photography methods. They are safe to use and less time consuming than other instrumented methods such as radiographic techniques which have ethical considerations.

Table 5.1 gives the summary of studies that have examined joint proprioception using purpose-built motorised devices. The lack of consistency in the manner in which the devices have been used makes comparison of studies problematic. The following section examines the limitations associated with the use of motorised devices.

## **5.2 Limitations of Motorised Devices for Assessing Joint Proprioception**

Knee angular displacement measurement using motorised devices has been calculated as the arctangent of the distance moved by the lateral malleolus divided by the length of the leg (Barrack et al. 1983ab; Skinner et al. 1984; Hall et al. 1994; Ferrell et al. 2004). This was based on the principle that the examined joint produces a simple arc of motion during assessment. However, it may be difficult for the knee joint axis of rotation to be correctly identified, for example where the joint is swollen. This may give rise to error in angular displacement measurement and as a result the validity of angular displacement calculation is questionable under such circumstances.



**Table 5.1: Summary of Studies that have used Motorised System for Assessing Knee Joint Proprioception**

<b>Authors</b>	<b>Population</b>	<b>Starting position (°)</b>	<b>Technique</b>	<b>Repeatability</b>	<b>Angular Velocity (°/s)</b>	<b>Remarks</b>
Barrack et al. (1983a)	12 healthy subjects (mean age 25 yrs)	Not reported	JPS	Not reported	10	Detail of method used for angular displacement determination not reported
Barrack et al. (1983b)	39 healthy and post operative patients (age range 24 -69 yrs)	90	JK JPS	Not reported	0.4 (JK) 10 (JPS)	Five test repetitions and no practice trials
Skinner et al. (1984)	29 healthy adults (age range 20 – 82 yrs)	60 90	JK JPS	Not reported	0.4 (JK) 10 (JPS)	Angular displacement calculated, ten test repetitions
Skinner et al. (1986)	11 healthy subjects (mean age 22.8 yrs)	60 90	JK JPS	Not reported	0.5 (JK) JPS not reported	Angular displacement calculated, five test repetitions and no practice trials,
Clark et al. (1996)	8 healthy subjects (mean age 34yrs)	Not reported	JK	Not reported	0.5	Chair had a limited adjustment, six trials, protractor incorporated, auditory input not eliminated
Friden et al. (1996)	39 subjects: 19 healthy 20 with ACL deficient knee (mean age 25 yrs)	Not reported	JK	Less variation in between day repeatability in healthy subjects	0.5	Sound imitating the step motor, specially designed protractor used by subject to assess their knee position, 95% confidence interval used for repeatability

**Table 5.1 (Continued)**

<b>Authors</b>	<b>Population</b>	<b>Starting position (°)</b>	<b>Technique</b>	<b>Repeatability</b>	<b>Angular Velocity (°/s)</b>	<b>Remarks</b>
MacDonald et al. (1996)	32 subject with ACL deficient and reconstructed knees (age range 15 to 41 yrs)	Not reported	JK	Not reported	0.5	Chair used had limited height adjustment, pressure of the air splint used was not measured
Borsa et al. (1997)	29 subjects with ACL deficient knees (mean age 28.7 yrs)	Not reported	JK	Test-retest (ICC = 0.92)	0.5	Earphones with white noise
Friden et al. (1997)	16 subjects with ACL deficient knees (mean age 26 yrs)	20 & 40	JK JPS	Not reported	0.5 10	Subjects in side lying with hip in semi flexion, ear phones with a sound imitating the motor, 3 practice trials
Beynnon et al. (1999)	20 adults with ACL deficient knees (mean age 40 yrs)	90	JK	Previously reported	Not reported	EMG used to ensure subject relaxation, practice trial administered
Rozzi et al. (1999)	34 healthy adults (mean age 19.6 yrs)	15	JK	Test-retest (ICC = 0.92)	0.5	Angular displacement calculation not reported
Grob et al. (2002)	30 healthy adults (mean age 41 yrs)	JK at 60, JPS at 90	JK JPS	Not reported	0.5 (JK) 12 for JPS practice trial 5 for JPS test trials	Subject in supine, number of practice trials not indicated, validity of angular displacement not reported, different angular velocities used for practice and test trials

**Table 5.1 (Continued)**

<b>Authors</b>	<b>Population</b>	<b>Starting position (°)</b>	<b>Technique</b>	<b>Repeatability</b>	<b>Angular Velocity (°/s)</b>	<b>Remarks</b>
Hassan et al. (2002)	68 Adults with osteoarthritis of the knee (mean age 66.6 yrs)	90	JPS	Test-retest (ICC = 0.74 to 0.96)	Not reported	One practice trial (passive) active JPS test
Roberts et al. (2003)	24 healthy adults (mean age 24 yrs)	Knee/ starting positions 20 & 40	JK	Not reported	0.5	Subjects laid on their side, tape recorder used to play imitating sound
Ferrell et al. (2004)	18 adults with HMS (mean age 27.3 yrs)	knee	JK	Between day repeatability (p = 0.15)	0.4	Ten repetitions (five moving into flexion and five moving into flexion). Method of statistical analysis used for between day repeatability not reported.
XU et al. (2004)	68 healthy adults (mean age 66.1 yrs)	45	JK	Not reported	0.4	Two practice trials, dominant limb assessed, headphones with white noise, angular displacement measured with electrogoniometer

Some authors such as MacDonald et al. (1996) incorporated a protractor goniometer to measure knee angular displacement during knee joint proprioception assessment in healthy adults and adults with ACL deficient knees using a motorised device. It was noted that the chair used by MacDonald et al. (1996) had limited adjustment for the participants' limb length. Limb length could be a function of a participant's height therefore; it might be difficult to align the knee joint axis of participants with the centre of rotation of the driving shaft of the motorised device. As a result, this method could be prone to measurement error of angular displacement of the knee joint.

Researchers such as Grob et al. (2002) used an electrogoniometer to measure joint angular displacement during knee joint proprioception assessment in healthy adults using a motorised device. Electrogoniometry may be a more accurate way to measure knee joint angular displacement than calculating the arctangent. However, as stated in section 4.7 electrogoniometers take time to calibrate and may therefore not be appropriate.

### **5.2.1 Repeatability**

In spite of the widespread use of motorised devices, there is limited information on the repeatability of their measurements. Only a few researchers have reported the between-days repeatability of knee joint kinaesthesia (JK) measurements in adults with ACL deficient knees (Borsa et al. 1997) and patients with HMS (Ferrell et al. 2004). The between-days repeatability of knee JK and JPS has been reported in healthy subjects (Friden et al. 1996). Ferrell et al. (2004) claimed that their device showed no statistically significant difference ( $p = 0.15$ ) between two measurement days (2 to 8 weeks apart). Friden et al. (1996) also reported no significant difference between repeated measurements of both JK and JPS taken (one month apart) in healthy adults. Similarly Borsa et al. (1997) demonstrated that their device had excellent test-retest repeatability ( $ICC = 0.92$ ) for JK measurement.

The above studies indicated that the results obtained from normal and symptomatic knee joints in adults remain statistically unchanged over several weeks. Since proprioceptive acuity in children is different from adults due to developmental changes (Goble et al. 2005), therefore, their findings may not be applicable to children. Additionally, Ferrell et al. (2004) analysed their data on between-days repeatability of knee JK by examining the mean difference between the data

collected on two measurement occasions and not the agreement between them. The lack of significant difference between measurements of 2 to 8 weeks apart may not necessarily indicate that the two measurements agreed (Bland and Altman 1986). As a result, their method should be viewed with caution. Further work is required to establish the repeatability of a motorised system in children.

### **5.2.2 Practice Trials and Test Repetitions**

The issue of practice trials and test repetitions should be addressed as it is believed that a one-off knee JPS assessment may lead to erroneous findings and may be misleading (Selfe et al. 2006). Only a few authors (Friden et al. 1997; Beynnon et al. 1999; Grob et al. 2002) in Table 5.1 made reference to an initial practice trial when examining knee proprioception in adults. Friden et al. (1997) administered three practice trials. Beynnon et al. (1999) did not state how many practice trials were administered in their study, while Grob et al. (2002) administered one trial but did not clearly justify this. Proprioception testing without initial practice trials may not be a true reflection of subjects' proprioceptive ability as familiarisation of the measurement procedure may not be accounted for (Marks 1994; Selfe et al. 2006).

Test repetitions in previous studies have ranged from five (Barrack et al. 1983b; Skinner et al. 1986; Hall et al. 1994) to ten (Ferrell et al. 2004). The basis on which these authors chose the number of test repetitions for proprioception assessment has not been reported. Multiple repetitions may be time consuming for proprioception testing in children and may cause them to lose concentration during assessment.

### **5.2.3 Starting Position and Subject Relaxation**

The subject's body position is crucial in clinical assessment of neuromuscular indices. Adequate relaxation of the subjects' test limb during proprioception testing may be affected. If the subjects' limbs are not adequately supported during proprioception testing, it may be difficult to eliminate proprioceptive inputs from the contracting muscles. Beynnon et al. (2000) reported that their subjects found it difficult or impossible to achieve complete relaxation of their lower leg musculature and remain passive during JPS testing.

Researchers such as Hall et al. (1994), Friden et al. (1996) and Ferrell et al. (2004) examined knee proprioception in a side-lying position by making the participants in their study lie on their contralateral side. However, in this position it may be difficult for the examiner to maintain a correct alignment of the joint axis in children in this manner. This may lead to measurement error.

Beynnon et al. (1999) acknowledged that lack of participant complete relaxation may be a limitation in the use of motorised devices for proprioception testing. Consequently, these authors used electromyography (EMG) to monitor electrical activity of muscles surrounding the knee joint in their study of knee JK in 20 adults with ACL deficient knees (mean age 40 yrs). EMG was not used in the present study of HMS in order to limit equipment intervention and to avoid possible interference of the motor (a component of the motorised device) on EMG activity.

#### **5.2.4 Elimination of External sensory cues**

Precautions have been taken by researchers to minimise proprioceptive input from external sensory cues to the examined joint when using motorised devices. For example, external cues may be visual, cutaneous and auditory. These precautions are discussed below.

##### **5.2.4.1 Cutaneous inputs**

It is believed that cutaneous sensation may have a role to play in JK (Macefield et al. 1990; Grigg 1994; Edin and Johansson 1995; Gilman 2002). Constant and intermittent pressure applied to the calf from an air splint inflated to 40 mm Hg has been found to produce changes in A- $\infty$  and A- $\gamma$  motoneurone excitability (Robichaud and Agostinucci 1996). Acknowledging this fact, cutaneous sensation has been minimised in previous studies of knee joint proprioception by means of inflated air splints (Hall et al. 1995; Ferrell et al. 2004) or woollen socks (Friden et al. 1996; Friden et al. 1997; Ageberg et al. 2007).

The pressure of the air splints used has varied between 20 mm Hg (Skinner et al. 1984; Xu et al. 2003) to 40 mm Hg (Hall et al. 1994) in previous studies. Some researchers such as MacDonald et al. (1996) and Grob et al. (2002) did not report the pressure of the air splints used in their studies. Although, there seems to be a good justification for the use of air splints during knee JK testing, Grigg (1994) was

of the opinion that cutaneous sensation may not have a significant role to play in JPS of proximal joints such as the knee.

Aside from the possible practical problems associated with the use of air splints in the clinical situation, it has been suggested that instead of preventing unwanted cutaneous receptor stimulation, airsplints may also stimulate muscle and articular pressure-sensitive proprioceptors (Stillman 2000). In addition, there was insufficient evidence to support their use in children as only one previous study (Barrack et al. 1983c) was found by the author of this thesis in which knee JK and JPS were tested with an air splint. Hence an air splint was not used in the present study.

#### **5.2.4.3 Auditory input**

Auditory input into proprioception has previously been minimised by some researchers during proprioception testing using motorised devices (Barrack et al. 1983a; 1983b; Skinner et al. 1986; Mallik et al. 1994; Hall et al. 1995). However, researchers like Clark et al. (1996) did not minimise auditory input in their study of knee JK in 8 healthy subjects (mean age 34 years). Investigators such as Borsa et al. (1997) have used earphones with 'white noise' while other researchers (Friden et al. 1996; Friden et al. 1997; Roberts et al. 2003) used earphones playing imitation sound from the stepper motor of their devices. The present author acknowledges the importance of minimising auditory input during proprioception testing. However, white noise and imitation sound may be sources of distraction to children during proprioception assessment (Taylor et al. 1998). Due to these reasons, earmuffs were used instead to minimise auditory input in children during proprioception testing in the present study.

This section has identified some possible problems associated with the use of motorised devices for assessing joint proprioception. To overcome some of these possible problems, a purpose-built motorised device was developed, along with a standardised protocol.

The rationale for the design of a purpose built motorised device for measuring proprioception in healthy children and children with HMS is provided in the following section. A detailed account of the developmental work and construction of a purpose-built motorised device is provided in the following section.

### **5.3 Development and Construction of a Purpose-Built Motorised Device**

In this section the construction of a purpose-built motorised device for assessing knee joint proprioception is examined.

#### **5.3.1 Components of the Motorised Device**

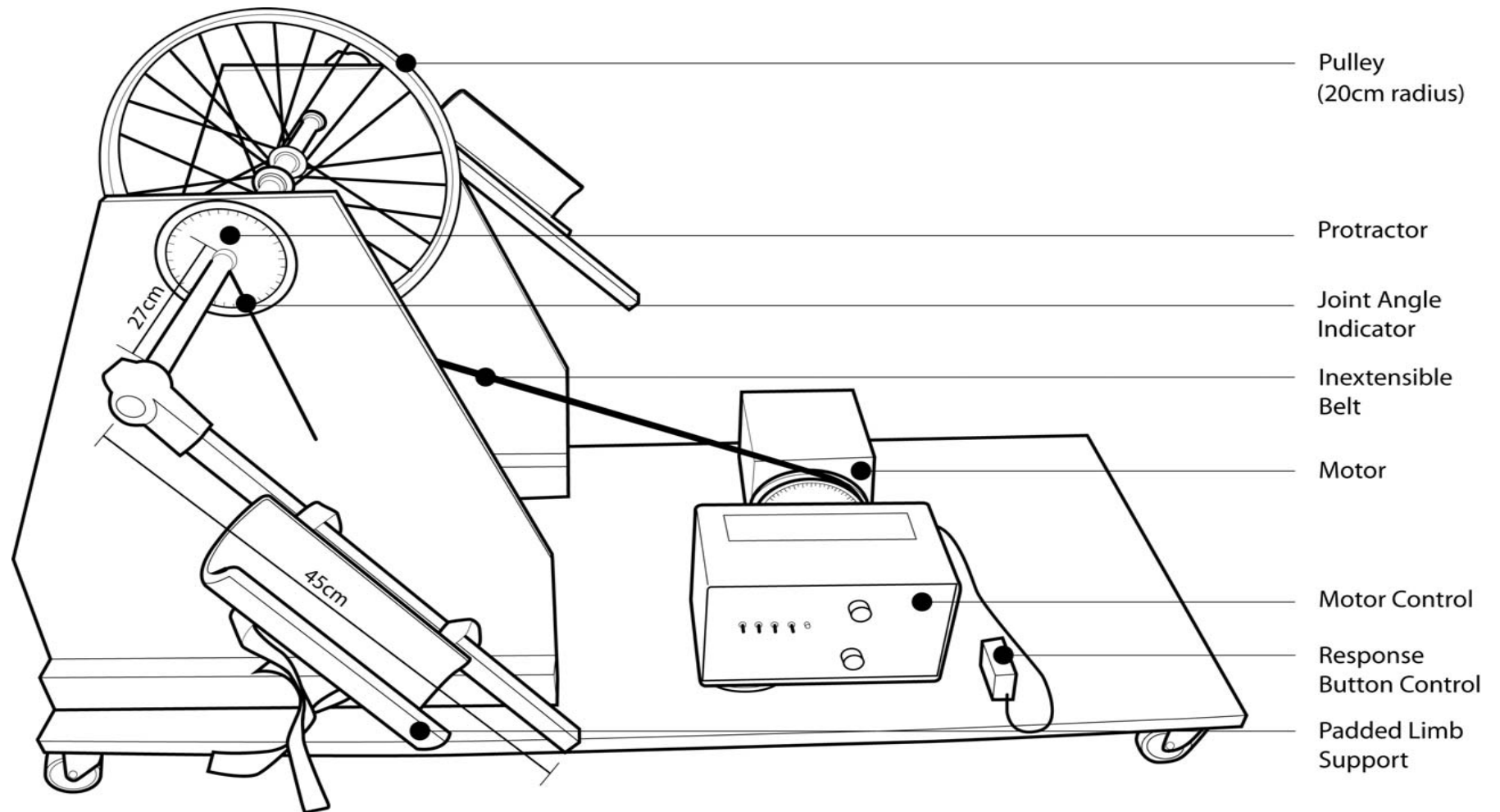
Automated Motion System PTY. LTD (Australia), the company that developed the motorised device used by Grob et al. (2002) for investigating knee joint proprioception in healthy adults was contacted. This company supplied the following components to the physiotherapy subject area, QMU, Edinburgh, UK: RTA GMD02 stepper drive (inc DIN connector), AMS RC10 clock card, SD 103-807-6341 stepping motor (with 2 meters screened cable), transformer (300VA) and power supply, speed control switch, relay and circuit board, TR MP-060-3-140-15-9.53-30-NEMA34.080 gearbox, (3 stage, 140:1 ratio, 15' backlash). A schematic circuit diagram and photographs of the device were also provided to QMU. The components were assembled with the assistance of the Chief Technician (QMU, Physiotherapy subject area), the Engineering Department of the University of Edinburgh, UK and George Brown and son Engineers, Edinburgh UK (a local engineering company) using the circuit diagram and photographs from Grob et al. (2002). The detailed account of the development is given below.

#### **5.3.2 Development of the Device**

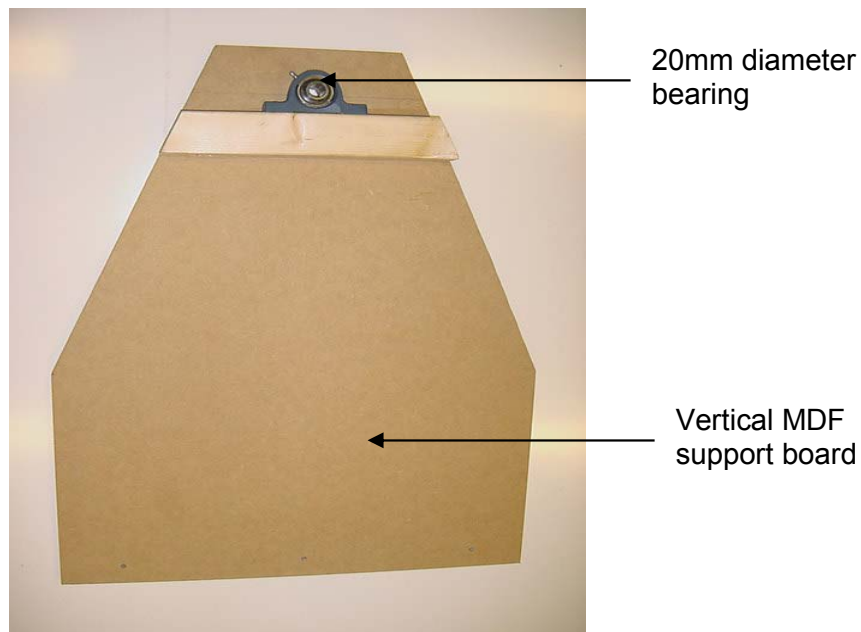
The motorised device (Figure 5.1) developed in this study moves the lower leg at a slow variable and constant angular velocity ( $0.08^{\circ}/s - 2.2^{\circ}/s$ ). It was made up of a slow-speed stepper motor mounted on a shaft, a motor control with a patient's response button, an inextensible belt and a 20cm radius pulley (adapted using a bicycle wheel). This was attached to a shaft of 100 cm long 20mm diameter (50cm long on either side of the wheel) (Figure 5.1).

To allow free movement of the shaft whenever the pulley was being driven, two bearings (20mm diameter) were attached to the vertical medium density fibre (MDF) wooden boards (approximately 64cm high) (Figure 5.2). The driving pulley and the wooden boards were all mounted on a mobile wooden platform. The developmental work carried out on the device was based on the author's clinical experience, and discussion with clinicians and academics in the field of proprioception and bioengineering.





**Figure 5.1: Schematic Diagram of the Purpose-Build Motorised Device (illustration by Steve Kelly, Manchester Metropolitan University)**



**Figure 5.2: Bearing Mounted on Wooden Board**

#### **5.3.2.1 Angular Displacement Measurement**

A number of options were considered for measuring angular displacement of the knee joint. These options are discussed below.

The use of a universal goniometer, electrogoniometer or VICON system was considered for measuring angular displacement in this study. Another option was to attach the driving shaft to the centre of the pulley, and then align the knee axis of rotation with the centre of rotation of the driving shaft with a protractor attached to the shaft. During a discussion between the present researcher and an expert in the field of proprioception (D. Xu, personal communication 01/07/2004) it was suggested that when the knee joint flexion-extension axis is aligned with the centre of rotation of the driving shaft the angular displacement of the shaft equals that of the knee joint. Due to the limitations associated with the use of manual goniometer; electrogoniometer and VICON (section 4.7) they were rejected by the researcher as means of measuring knee angular displacement during proprioception testing in the present study.

A simple protractor is an inexpensive tool for measuring angular displacement, easy to use and time efficient. Moreover, it is a valid and accurate means of measuring ROM. It was with these concepts in mind that more focused developmental work was carried out to incorporate a protractor for measuring knee angular displacement during proprioception testing in this study. A simple protractor scale with 1° increments was attached to the wooden boards (Figure 5.1). For ease of measurement, a pointer was attached to both ends of the shaft.

### **5.3.2.2 Starting Position**

Subject positioning and relaxation of the examined joint was considered after the initial development of the device. Based on previous work on proprioception and discussion with experts in the field, the following were the possible options:

- 1 Side lying (Friden et al. 1997; Ferrell et al. 2004).
- 2 High sitting without limb support and the contralateral knee joint bent to 90° and the foot resting on a stool.
- 3 Supine lying with both lower legs freely hanging at the edge of a plinth (Barrett 1991).
- 4 High sitting with back reclined to 60° (to encourage relaxation) with both lower leg freely hanging at the edge of a plinth (Barrack et al. 1983c; Skinner et al. 1984; Tsang and Hui-Chan 2003) and the test limb placed in a limb support.

The first three options were rejected because of the reasons already discussed in section 5.2. However, the last option appeared to be more suitable for proprioception assessment in children as the researcher believed that children were likely going to find the position comfortable. In addition, this option was chosen to allow comparison with the only previous study available on knee joint proprioception in children (Barrack et al. 1983c). Moreover, it was felt that the position was going to enhance adequate relaxation of the examined limb. Consequently, the researcher adopted the last option as the testing position.

### **5.3.2.3 Lower Limb Support**

To construct a lower limb support, three options were considered by the investigator. These options were either to use a hinged knee brace, controlled passive movement (CPM) frame or polyvinyl chloride (PVC) drainpipe. A hinged knee brace was rejected because it has been previously demonstrated that knee joint proprioception is enhanced by application of a neoprene sleeve (Birmingham et al. 2000). As a result, the researcher felt that using a hinged knee brace might give confounding results on proprioceptive ability of children in this study. The CPM frame (Homecraft, Ashfield, England) but was found to be too large for use with children. Instead a purpose-built limb support was constructed using a PVC drainpipe. This was attached to a piece of aluminium frame (45 cm long) each that were separated by a distance of 27cm on either side of two MDF (2cm thick) wooden boards. The limb support was padded with closed cell rubber (6mm thick) (Footman, England). Velcro straps were also attached to each limb support.

### **5.3.2.4 Sound Proofing**

During the initial pilot work, it was discovered that the stepper motor of the device was noisy and could be a source of distraction to children during testing. A sound proofed box was therefore provided for the stepper motor by a local engineering company (Christie LTD, Edinburgh). The noise reduced considerably and was minimal with the use of ear muffs.

### **5.3.3 Summary**

This section has examined the various studies that have used motorised devices for assessing joint proprioception. The advantages of a purpose-built motorised device have been discussed. In addition, the possible limitations associated with the use of motorised devices in children have been highlighted.

The construction work of the device has been discussed in this chapter. For any measuring instrument to be clinically accepted, validity and repeatability of its measurements must be tested. Therefore, a series of experiments were carried out to examine the criterion-related validity and repeatability of the newly developed motorised system.

The next section presents validation experiments carried out on the purpose-built motorised device.

## **5.4 Equipment Validation**

Measurement tools are important elements of both clinical and research assessments (Bower and Ashburn 1998). Clinical measures are used to provide continual re-evaluation of effectiveness of treatment intervention and assess the ongoing progress or regression of patients (Romain 1993). For any measuring tool to provide meaningful information, its measurement must be valid and repeatable (Domholdt 2000). Durward et al. (1999) stated that some equipment lacks validity and repeatability, thus limiting the generalisability of their measurements. Measurement tools can help to demonstrate the effectiveness of treatment in children with neuromuscular impairments, activity limitations and participation restrictions. Despite the availability of measurement tools, the choice of appropriate equipment can be difficult (Jette 1995). Before any measurement tool can be used in trials some basic properties of the tool must be established (McGrath et al. 1996).

The issues related to calibration, accuracy and validity of the measurement tools used in this study are explored in this section. Investigations related to the validity of the measuring tools are also discussed.

### **5.4.1 Calibration**

If a measuring tool is to be used we need to know how the output of the device relates to the input. Some instruments are pre-calibrated at the time of manufacture and there should be a direct relationship between the input and output such that the measured and reference values are identical (Durward et al. 1999). It is worth checking that a pre-calibrated instrument is responding properly as the response may change with time and the device may be damaged or faulty (Durward et al. 1999). Calibration tests were carried out to establish the accuracy and validity of each piece of equipment (myometer, universal goniometer and motorised device) used in the present study.

#### **5.4.1.1 Accuracy**

Accuracy of an instrument is the differences between 'true' and 'measured' values (Durward et al. 1999). This can be referred to as 'systematic error' (Allard et al. 1995). The accuracy of a device is expressed by the error reading between the measured value and the reference value and was determined for the instruments used in the present study.

### 5.4.1.2 Validity

According to Domholdt (2000) validity is the degree to which an instrument measures what it is purported to measure; the extent to which it fulfil its purpose. Validity of a measurement refers to how well the measurement represents the true value of the variable that is being measured. For example, the purpose of goniometry is to measure joint angle (ROM) (Norkin and White 2003). Therefore, a valid goniometric measurement is one that truly represents the actual ROM.

Validity also deals with the accuracy of inferences made from measurements. It requires independent knowledge of the 'true' value of the variable being measured and it is concerned with the relationship between the measurement and the outcome being measured. It is believed that validity is not an inherent property of an instrument but rather an attribute of a measurement (Sim and Arnell 1993).

There are four main types of validity (Sim and Arnell 1993): criterion-related validity, content validity, face validity and construct validity. These are discussed below.

**a) Criterion-related Validity:** The criterion-related validity of an instrument justifies its validity and can be examined by comparing its measurements with a well-established measurable criterion that is acceptable as the standard indicator of a concept (*gold standard*) of measurement (Sims and Arnell 1993). An instrument that gives an accurate representation of the concept or variable, demonstrates criterion-related validity. Criterion-related validity can be classified into three: concurrent validity, predictive validity and prescriptive validity.

**b) Content Validity:** Content validity determines whether or not an instrument adequately measures and represents the domain of content (the substance) of the variable being measured. Content validity involves more rigorous and careful consideration; it is based on subjective opinion (Norkin and White 2003).

**c) Construct Validity:** A measure has construct validity if it relates to the theoretical considerations of what is purported to be measured with the actual methods and tools being used. It is the hypothetical argument for the measurement tool (Domholdt 2000).

**c) Face Validity:** A measure has face validity if the measure is judged appropriate for the behaviour being measured (Domholdt 2000).

The validation experiments carried out in the present study are presented in the next section.

## **5.5 Validation Experiments**

### **5.5.1 Background**

Before data could be collected on the movement of the knee joint, knowledge of the measurement characteristics of the measuring tools was necessary. Since data was collected during a single session, at different times of the day and between days, it was necessary to ensure that the findings of every piece of equipment were repeatable during and over these periods. Therefore, the criterion-related and repeatability validity of the digital myometer and universal goniometer used in this research was investigated on two different occasions (morning and afternoon) and on two different days (one week apart). These times were chosen to reflect when data was collected in the present study.

#### **Myometer and Universal Goniometer**

The fixed digital myometer (MIE Ltd, Leeds, England) is a device pre-calibrated by the manufacturer. Seniorou et al. (2002) reported good test-retest repeatability of this myometer in healthy children and children with cerebral palsy (CP) (section 3.5.5.2). Additionally, van der Linden et al. (2004) have also demonstrated a good to excellent test-retest repeatability (average of 6 days apart) of the myometer in healthy children and those with CP (section 3.5.5.2). Although the myometer was pre-calibrated by the manufacturer, there were no studies found on its validity. Additionally, it was not known if the myometer readings would vary over time. Therefore, experiments were conducted to investigate the criterion-related validity and repeatability (within-day and between-days) of the force measurement by the myometer. The validity and repeatability of the angular measurements of the universal goniometer were also examined.

Known weights (as recorded by a weighing scale) were used to validate the myometer, while a Myrin goniometer was employed to validate the universal goniometer. Intra class correlation coefficient (ICC) and 95% limits of agreement (LOA) were used to determine the criterion-related validity, within-day and between-days repeatability of these measuring tools (Rankin and Stokes 1998). The results of the experiments (validation and repeatability) are presented in Appendix 1.

High ICC values (ranged = 0.92 to 1.00) were obtained for all the measurements (Appendix 1). In addition, LOA demonstrated small amount of variation between the measurements obtained from the myometer and weighing scale. It also showed little variation between repeated measurements (both within-day and between-days) by the myometer. LOA also revealed small instrumental variation between the universal and Myrin goniometers. Low within-day and between-days measurement error using the universal goniometer was also observed. These findings suggested that both the myometer and universal goniometer were accurate and valid for measuring force and angles respectively. They also indicated good agreement between repeated measurements by the myometer and universal goniometer. It is hereby acknowledged that these validation and reliability experiments were bench tests, and may therefore not be directly applicable to clinical measurement in human subjects. However, the findings suggest that the digital myometer and universal goniometer are valid and repeatable instruments and were therefore used for assessing knee muscle torque and passive ROM respectively.

### **Motorised Device for Assessing Joint Proprioception**

The need for a purpose-built device for JK and JPS assessment has been discussed in sections 4.7. Although many researchers (Barrack et al. 1983c; Skinner et al. 1984; Corrigan et al. 1992; Grob et al. 2002) have used motorised devices for assessing knee joint proprioception, very little is known about the accuracy and validity of the angular velocity and angular displacement of these devices. In order to determine the suitability of this instrument for this study and to ensure that it provided accurate, valid and repeatable data, a series of experiments were conducted to test its criterion-related validity and between-trials repeatability. Criterion-related validity of the motorised device was investigated as it helps to determine its appropriateness by comparing the measures with an existing instrument measuring the same criterion (Gomm et al. 2000).



The detailed accounts of the validation and repeatability experiments on the motorised device are provided in the following sections.

## **5.6 Calibration, Validation and Pilot Experiments on the Purpose-built Motorised Device**

The use of motorised devices for assessing knee joint proprioception is becoming popular (Grob et al. 2002; Hassan et al. 2002; Roberts et al. 2003; Xu et al. 2003; Ferrell et al. 2004; Friden et al. 2006; Ageberg et al. 2007). Despite the wide use of these devices, their accuracy and the criterion-related validity of the angular velocity and lower leg displacement have not been reported. It is possible that the angular velocity of motorised devices and lower leg displacement by this device are inaccurate and invalid. This section explores issues related to the accuracy and criterion related-validity of angular velocity and angular displacement of the purpose-built motorised device. It also examines the between-trial repeatability of knee JPS assessment in healthy subjects using the device.

### **5.6.1 Experiment 1: Angular Velocity Calibration Test of the Proprioception Device Stepper Motor**

#### **5.6.1.1 Background**

The angular velocity of a slow speed stepper motor used for the purpose-built motorised device was pre-calibrated by the manufacturer (Automated Motion Systems PTY. LTD. Australia). Hence, this experiment was aimed at testing the accuracy of that angular velocity.

#### **5.6.1.2 Methods**

The accuracy of the angular velocity of the motor was tested using a digital stop clock (MIE, Medical Research Ltd, England) and a video camera recorder (M3000 Panasonic, Japan). The device and digital stop clock were placed next to each other on a table (135 cm high) and were both set at zero (degrees and seconds respectively). Then, the video camera recorder was mounted on an adjustable tripod stand to the same height (135cm), directly in front of the table. This was done to ensure that the video camera was able to capture and record both movement of the stepper motor pulley (7.5cm diameter) and the time on the stop clock. They were both displayed on a 24 inch television set (Samsung, Japan).

At the start of the test, the recording button of the video camera was switched on. Then, the pulley of the stepper motor was set to rotate between  $0^{\circ}$  and  $100^{\circ}$  at each of the 12 pre-calibrated angular velocities of the stepper motor, ranging from  $0.2^{\circ}/s$  to  $6^{\circ}/s$  (0.2, 0.3, 0.4, 0.5, 0.6, 0.8, 1, 2, 3, 4, 5, 6) in a randomised order. It would have been better to use a timed switch that could control the device and stop clock simultaneously. However, due to time constraints this was not used, instead the device and the digital stop clock were both switched on simultaneously by the researcher. Once the device reached  $100^{\circ}$ , the device and the stop clock were both stopped immediately. The time taken (as displayed on the digital stop clock) by the pulley of the device to rotate through  $100^{\circ}$  was recorded at each angular velocity. This procedure was performed three times for each angular velocity. The average of the three readings by the digital stop clock was calculated as the time taken for the device to rotate through  $100^{\circ}$ . The angular velocity was calculated by dividing the angular rotation (degrees) by the time (seconds) using the formula below:

$$\text{Angular velocity (AV)} = \frac{\text{Angular rotation } (^{\circ})}{\text{Time (s)}} \quad \text{Equation 5.1}$$

The agreement between the angular velocity of the device and the measurements obtained from the stop clock was examined using ICC and limits of agreement (Rankin and Stokes 1998).

### 5.6.1.3 Results

The angular velocity of the device and the measured values obtained from the stop clock are illustrated in Figure 5.3a. The Bland and Altman plot of agreement between the mean angular velocity of the two devices and their difference is shown in Figure 5.4. Figure 5.3a shows a linear relationship between the angular velocity of the two device and that derived from the stop clock. From Figure 5.4, the mean difference between the devices was small ( $0.01^{\circ}/s$ ). Additionally 95% limits of agreement revealed that the confidence interval of the mean difference between the devices range between  $-0.06^{\circ}/s$  to  $0.07^{\circ}/s$ . Moreover, this figure revealed that in all cases but one, the difference between the angular velocity obtained from both devices was within the 95% confidence interval. Furthermore a high ICC value of 1.00 was obtained between the measuring devices.

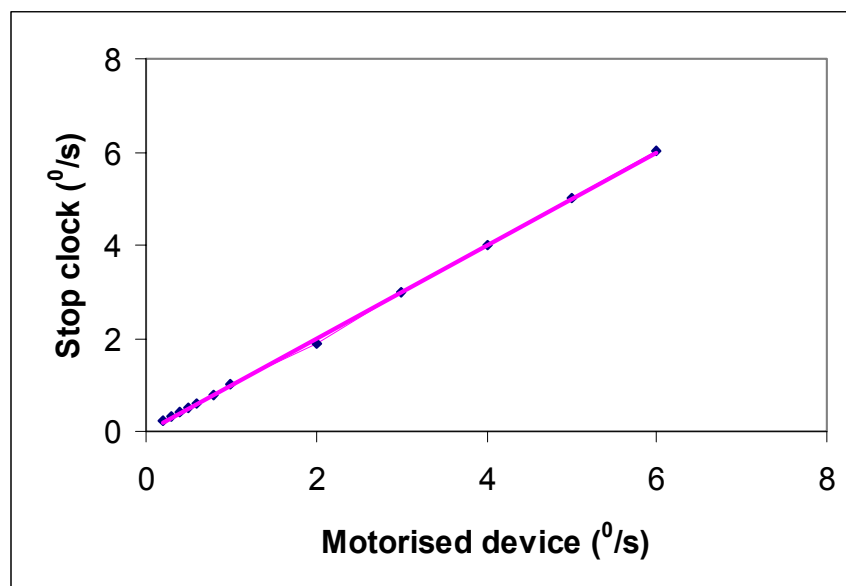


Figure 5.3: Angular Velocity of the Motor Plotted Against angular velocity derived from the Stop Clock.  $Y = a + bX$ ; where  $Y$  = predicted score,  $a$  = intercept constant and  $b$  = regression coefficient.

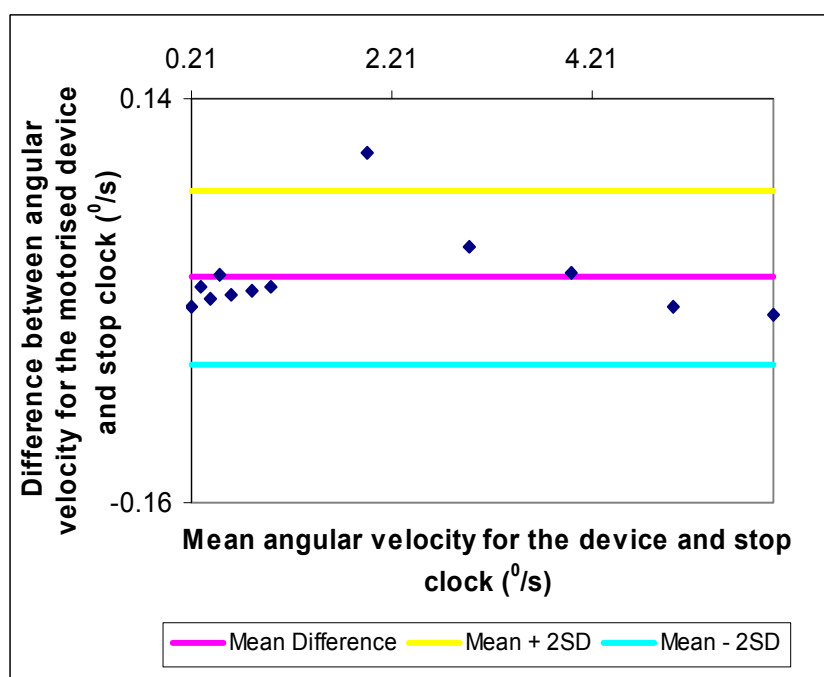


Figure 5.4: Bland and Altman Plot of Agreement between Mean Angular Velocity of the two Devices

#### **5.6.1.4 Discussion**

The intraclass correlation coefficient (ICC) is a measure of relative error which includes systematic bias while LOA can be used to calculate absolute agreement expressed in the unit of measurement (Rankin and Stoke 1998; Bland and Altman 1986). LOA provides a 95% range of error for two instruments, i.e. a real change between them which will be outside the LOA. The smaller the range, the better the agreement is between the methods (Bland and Altman 1986). LOA revealed that the mean difference between the angular velocities of the two devices was around zero and was included in the 95% confidence interval. This suggests that there was no systematic change in the mean angular velocities measured by the devices. In addition, the range of LOA was small, thus implying that there was a low random error in the angular velocity of the motorised device. It is possible that there could have been human error in the way the device and the stop clock were controlled by the researcher which could be avoided in the future by using a timed switch. However, the results of this experiment showed that there was an excellent agreement between the angular velocities obtained from the two devices. Therefore, this experiment suggests that the angular velocity calibration of the stepper motor for the purpose-built motorised device was accurate.

#### **5.6.1.5 Conclusion**

Given the results of this experiment it would appear that the slow speed motor can be used to produce constant angular velocity with minimal systematic and random errors. The author therefore accepted the purpose built motorised device as a valid and accurate instrument that can be used to produce constant angular velocity.

### **5.6.2 Experiment 2: Criterion-related Validity of Angular Velocity of the Limb Support (under an unloaded condition)**

#### **5.6.2.1 Background**

In section 5.2 the researcher justified the need for the development of a purpose-built motorised device for assessing JK and JPS. The previous section (5.6) has demonstrated that the angular velocity of the stepper motor was accurate. The motor was specially adapted for use in the present study. Since the radius of the pulley (20cm) which the limb support was attached to was different from that of the stepper motor (7.5cm) it was envisaged that the angular velocity of the the limb support would be different. This experiment was designed to determine the angular velocity of the limb support.

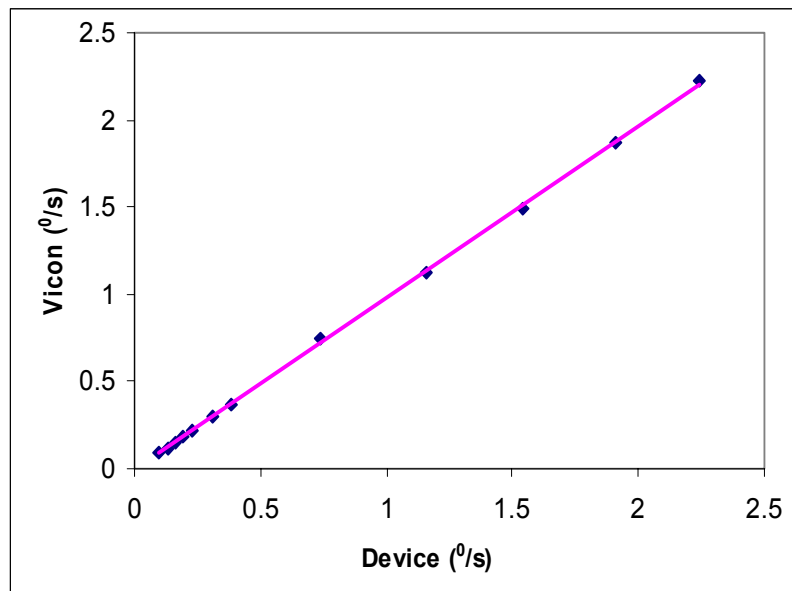
### 5.6.2.2 Methods

The angular velocity of the limb support was validated using the VICON camera system and a universal goniometer (Jamar, USA). Two 50cm plastic rulers were attached to the universal goniometer (one to each arm), using a double-sided tape (Niceday, UK). The VICON camera system was calibrated. Then, three reflective markers (14mm diameter) were attached to the goniometer using the double-sided tape (one to the centre of the goniometer and one each to the distal end (5cm) of the attached rulers). The immovable arm of the goniometer was aligned with the edge of an adjustable plinth and attached to it using double-sided tape. The centre of the goniometer was aligned with the centre of rotation of the driving shaft of the motorised device and was secured to it using double-sided tape. The moveable arm was attached to the limb support such that it was in alignment with the aluminium frame.

At the start of the test, the device was set to rotate from  $0^{\circ}$  to  $100^{\circ}$  at 12 specified angular velocities on the stepper motor ranging from  $0.2^{\circ}/s$  to  $6^{\circ}/s$  (corresponding to approximately  $0.08^{\circ}/s$  to  $2.2^{\circ}/s$  of the limb support) in a randomised order. Once the device reached  $100^{\circ}$ , the device and the VICON were both stopped immediately. The measurement was taken three times and the mean time taken by the device to rotate at each angular velocity through  $100^{\circ}$ , as captured by the VICON was calculated. Data analysis was same as in section 5.6.1.2.

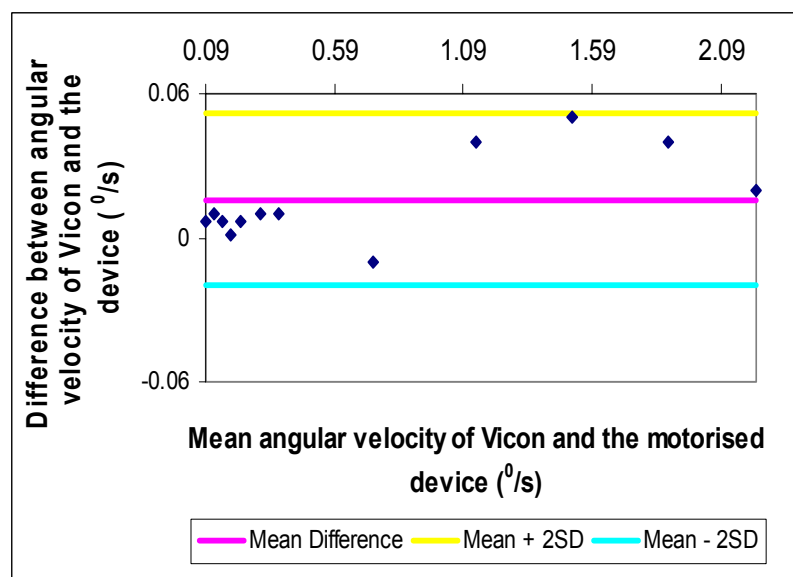
### 5.6.2.3 Results

The relationship between angular velocity of the motorised device and the measured values obtained from VICON are shown in Figure 5.5. The relationship between the mean angular velocity of the two measuring devices and their difference is illustrated in Figure 5.6. The mean difference between the devices was  $0.02^{\circ}/s$ . 95% limits of agreement revealed that the confidence interval of the mean difference between the devices range between  $-0.02^{\circ}/s$  to  $0.05^{\circ}/s$ . A high ICC value of 1.00 was obtained between the measuring devices. The results also showed that the ratio of the angular velocities of the limb support to those of the stepper motor was approximately  $1^{\circ}/s:2.67^{\circ}/s$ .



**Figure 5.5: Angular Velocity of the Device (Unloaded) Plotted Against VICON.**

$Y = a + bX$ ; where  $Y$  = predicted score,  $a$  = intercept constant and  $b$  = regression coefficient.



**Figure 5.6: Bland and Altman Plot of Agreement between the Mean Angular Velocity of VICON and the Device with a Larger**

#### **5.6.2.4 Discussion**

The results of this experiment showed an excellent agreement existed between the angular velocity of the limb support and that measured by the VICON. LOA revealed that the mean difference between the angular velocities of the devices was around zero and within the 95% confidence interval. This implies that a low systematic error was observed in the angular velocities measured. The range of LOA was small and suggests that there was a low random error in the angular velocity of the motorised device. These findings therefore, suggest a high degree of accuracy of the angular velocity of the purpose-built motorised device after modification. The lower angular velocity values recorded for the limb support were due to the larger pulley used for the limb support. This suggests that the limb support will require more time to move through a specified angular distance than the stepper motor.

#### **5.6.2.5 Conclusion**

The findings of this investigation demonstrated that the angular velocity of the slow speed motor after modification was accurate suggesting that the device can be used to produce angular velocity with minimal systematic and random errors. It is acknowledged that constant angular velocity of the motorised device was not validated over time period in the present study therefore it is unknown whether there were any inertia effects on the device or not. Given this reason, it possible that the method used in this experiment produced data on average speed. In a future study, it might be useful to check whether motorised devices produce constant angular velocities by using the VICON system or electrogoniometer. Based on the assumption that motorised devices are designed to produce constant angular velocity and because of the findings of the present experiment, the investigator accepted the purpose-built motorised device as a valid and accurate instrument that can be used to produce constant angular velocity. Therefore, it was important to determine the accuracy of the angular velocity of the device when used to lift humans' lower limbs.

### **5.6.3 Experiment 3: Criterion-related Validity of Angular Velocity of the Limb Support with Human Limbs in Situ**

#### **5.6.3.1 Background**

Experiments 1 and 2 above demonstrated that the angular velocity calibration of the motorised device before and after modifications was accurate. It was possible that the angular velocity of the device would change when under a loaded condition, such as when it is being used to move a human lower limb. Therefore, this experiment was designed to determine the accuracy and criterion-related validity of angular velocity of the device with human limbs in situ.

#### **5.6.3.2 Methods**

Four healthy subjects (2 adults and 2 children, mean age  $26 \pm \text{SD } 12.7$  years) were recruited from the students and children of staff of the University, following ethical approval from QMU Ethics Committee. Informed written consent was obtained from the participants. The test limb was determined in a randomised order by telling each subject to pick a piece of paper from an envelope containing two pieces of paper (each piece had right or left written on it). Subjects sat on an adjustable plinth with their lower legs hanging freely and knee joint in  $90^\circ$  flexion. The lateral knee joint axis (femoral condyle) was located and was aligned with the centre of rotation of the driving shaft of the device (Marks 1994; Xu et al. 2004). The subject's lower leg was supported in a padded limb support and was secured with Velcro straps. The Experimental set up was similar to Figure 5.9 in section 5.6.6. A pilot study revealed a significant angular measurement error when the VICON system was used to validate the angular velocity of the device under the loaded condition. This error was believed to be due to skin movement that may be associated with marker placement. As a result, the VICON system was rejected and a digital stop clock (MIE Ltd, Leeds, England) and the device's protractor were used to validate angular velocity in this experiment.

At the start of the test, the motorised device moved the test limb from a pre-determined angle of  $90^\circ$  of knee flexion to  $0^\circ$  at each angular velocity ranging from approximately  $0.08^\circ/\text{s}$  to  $2.2^\circ/\text{s}$  on the limb support (corresponding to  $0.2^\circ/\text{s}$  to  $6^\circ/\text{s}$  on the stepper motor) in a randomised order. Once the device reached  $0^\circ$ , the device and the clock were both stopped immediately. The measurement was taken three times and the mean time taken by the limb support to move (with the subject's limb in situ) at each angular velocity through  $90^\circ$ , as recorded by the clock was



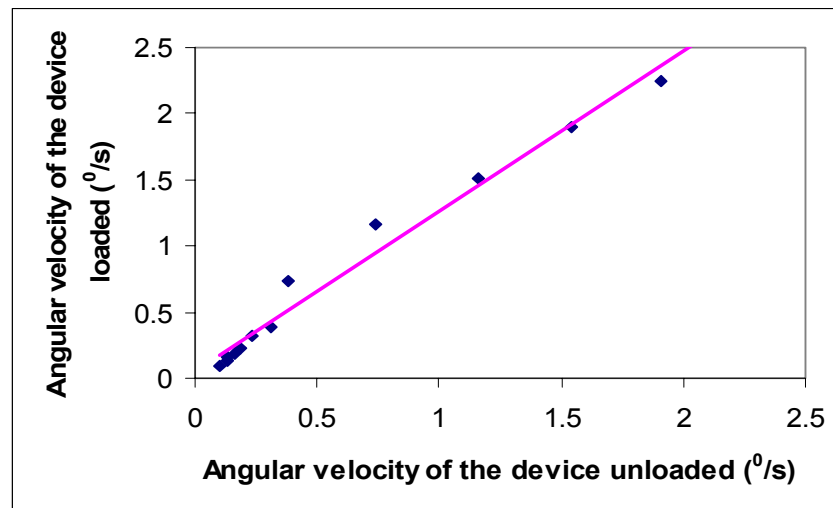
calculated. The procedure was the same as in section 5.6.2 except that the limb support was in situ in this experiment. Data analysis was also the same as in section 5.6.2. The starting angle of 90° knee flexion was chosen as knee JPS test had been tested using this starting angle (Carter et al. 1994; Hurley et al. 1998; Selfe et al. 2006).

### 5.6.3.3 Results

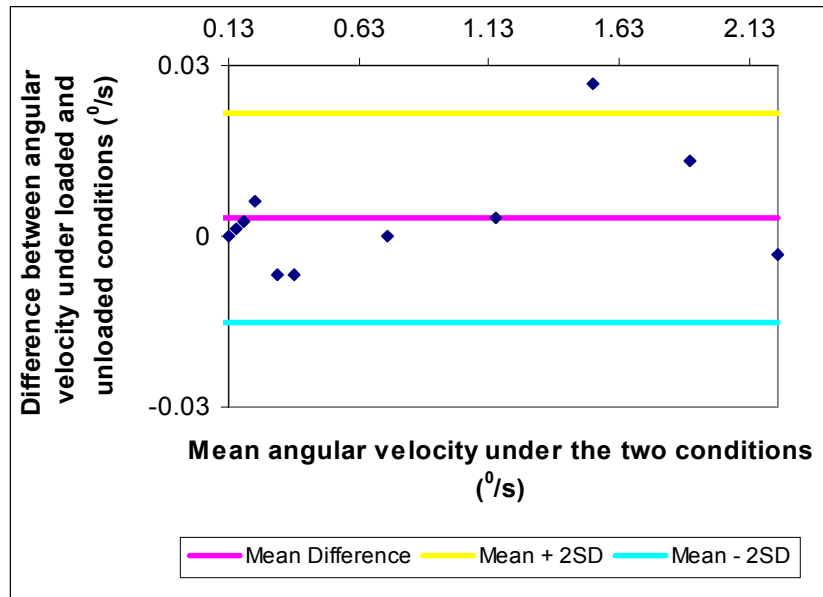
Table 5.2 displays the characteristics of the participants. Angular velocity of the motorised device under unloaded and loaded conditions is shown in Figure 5.7. Bland and Altman plots of agreement between the mean angular velocity of the device under these conditions and the differences between the conditions are illustrated in Figure 5.8. The mean difference of the angular velocity was 0.003°/s. 95% LOA revealed that the confidence interval of the mean difference between the two conditions ranged from -0.02°/s to 0.02°/s. An ICC value of 1.00 was obtained between the two conditions.

**Table 5.2: Characteristics of the Participants (n = 4; 2 adult and 2 children)**

	Age (years)	Weight (kg)	Height (cm)
Mean	26	59	160.3
SD	12.7	23.4	20.9
Range	8 - 37	30 - 84	130 - 176



**Figure 5.7: Angular Velocity of the Motorised Device Under Loaded and Unloaded Conditions.  $Y = a + bX$ ; where  $Y$  = predicted score,  $a$  = intercept constant and  $b$  = regression coefficient.**



**Figure 5.8: Bland and Altman plot of agreement between the mean angular velocity under unloaded and loaded conditions**

#### 5.6.3.4 Discussion

The results of this experiment showed that the angular velocity of the motorised device when loaded with human lower limbs was valid and accurate. LOA revealed that the mean difference between the angular velocities under the two conditions (loaded and unloaded) was around zero and within the 95% confidence interval. This suggests that there was no systematic change in the mean angular velocities measured under the two conditions. LOA was also found to be small suggesting that there was a low random error in the angular velocity under the two conditions. Therefore, this investigation suggests that the angular velocity of the purpose-built motorised device when loaded with subjects' lower limbs was accurate and valid. Since the magnitude of error under these conditions was marginal, it can be assumed that the motorised device is capable of producing constant angular velocity under these conditions.

### **5.6.3.5 Conclusion**

This experiment provides evidence that the angular velocity of a purpose-built motorised device, when loaded with human lower limbs was valid and accurate. Based on this investigation the device has the ability to be used to move human lower limb at a constant angular velocity during joint proprioception assessment. Given the findings of this experiment, the investigator accepted and used the device for examining human knee joint proprioception. Therefore, to establish the clinical utility of this device for assessing JK and JPS, the criterion-related validity of its angular displacement was investigated as reported in the following section.

## **5.6.4 Experiment 4: Criterion-related Validity of Angular Displacement of the Limb Support (Unloaded)**

### **5.6.4.1 Background**

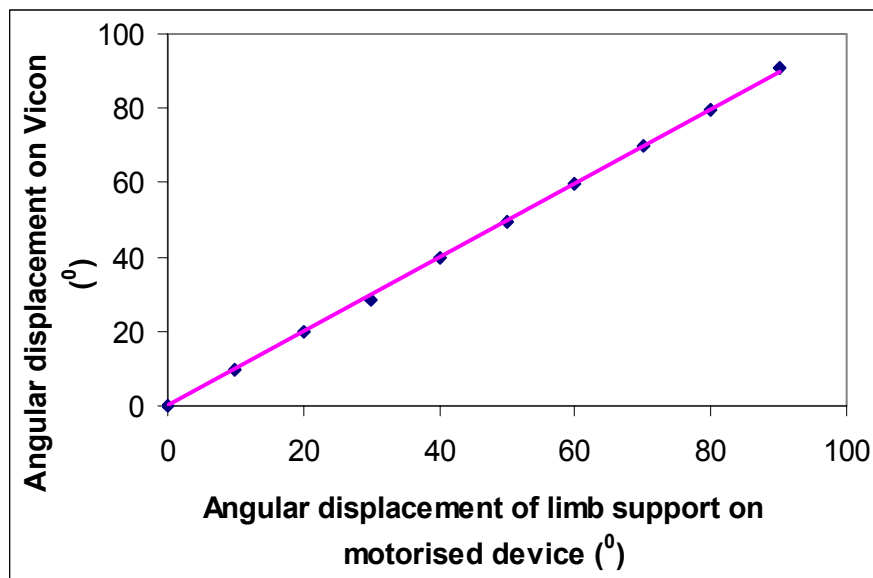
Previous experiments (1, 2, and 4) have shown that the angular *velocity* of the motorised device before modification, unloaded and loaded was accurate. However, for the measurements of this device to be considered valid, it must be able to measure what is purported to measure. There was the possibility that angular *displacement* of the motorised device might not have been accurate due to its modification. Therefore, the criterion-related validity of angular displacement of the limb support was investigated.

### **5.6.4.2 Methods**

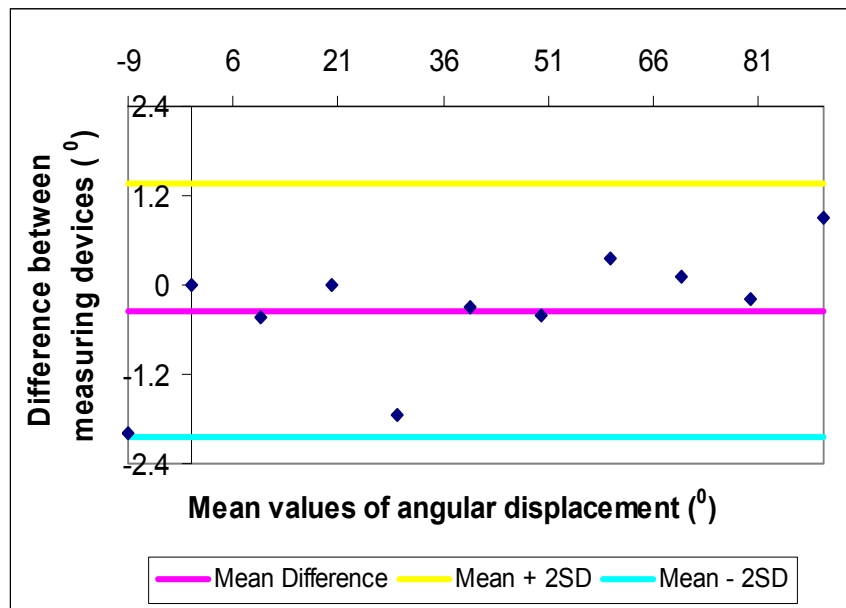
The validity of angular displacement of the limb support was established using the VICON camera system and a universal goniometer (Jamar, USA). The experimental set-up including marker placement was the same as in section 5.6.2. The VICON camera system was used to capture the set-up and the angle on the universal goniometer was recorded. Thereafter, the moveable arm of the goniometer was moved by the device from a starting position of  $90^{\circ}$  to 10 pre-determined angles (ranging from  $90^{\circ}$  to  $-10^{\circ}$  in  $10^{\circ}$  increments) at each specified angular velocity ranging from  $0.08^{\circ}/s$  to  $2.2^{\circ}/s$  in a randomised order. Once the device reached the pre-determined angle, the investigator stopped the device using the response button. Then, the VICON was used to capture the universal goniometer in that position. This procedure was performed three times for each angle. The average of the three readings (angular displacement) captured by the VICON calculated by polygon (VICON software) was taken as the angular displacement. Data analysis was same as in section 5.6.2.

### 5.6.4.3 Results

The angular displacement of the motorised device and VICON are demonstrated in Figure 5.9. Figure 5.10 shows the Bland and Altman plot of agreement between mean angular displacements of the two devices and the difference between them. From Figure 5.6b, the mean difference between the devices was small ( $-0.34^{\circ}$ ). Additionally, from this Figure (5.6b) 95% LOA revealed that zero lies between the 95% confidence interval ( $-2.04^{\circ}$  and  $1.37^{\circ}$ ) of the mean difference between the measuring devices. The angular displacement of the VICON system was sometimes higher than that those of the motorised device. Furthermore, a high ICC value ( $ICC = 0.96$ ) was obtained between the measuring devices.



**Figure 5.9: Angular displacement of limb support (unloaded) plotted against VICON.  $Y = a + bX$ ; where  $Y$  = predicted score,  $a$  = intercept constant and  $b$  = regression coefficient.**



**Figure 5.10: Bland and Altman plot of agreement between angular displacement and the differences between the measuring devices.**

#### 5.6.4.4 Discussion

LOA revealed that the mean difference between the angular displacement on the VICON and the universal goniometer was around zero and within the 95% confidence interval. This implies that there was no systematic change in the mean angular displacement measured by the devices. The range of LOA was small and suggests that there was a low random error in the angular displacement of the lower limb support as measured by the universal goniometer and the VICON. Given these findings, the experiment showed an excellent agreement between the angular displacements measured by the two measuring devices. Using the VICON as a gold standard, the results revealed a low measurement error. This suggested that a high degree of accuracy of angular measurements can be obtained using the purpose-built motorised device.

#### 5.6.4.5 Conclusion

This investigation demonstrated that angular displacement of the purpose-built motorised device was accurate. Based on the results, it appears that angular displacement of the limb support during knee joint proprioception assessment may be accurate with minimal error. It seems that the device could be used for knee angular displacement measurement during proprioception assessment. Therefore, it was used by the researcher in the present study to determine JK and JPS in healthy children and children diagnosed with HMS.

## **5.6.5 Experiment 5: Validity of the Angles of a Photocopied Protractor**

### **5.6.5.1 Background**

Experiment 4 above showed that there was an excellent agreement between the VICON camera system and the motorised device for measuring angular displacement under an unloaded condition. For purpose of standardisation and ease of measurement of angular displacement during JK and JPS assessment, the protractor for the universal goniometer previously validated (see Appendix 5.2) was photocopied and attached to the outer part of each wooden board of the motorised device. The incremental angle of the photocopied protractor might have been altered during the process of photocopying. Hence, this experiment was aimed at investigating the accuracy of the photocopied protractor (PP).

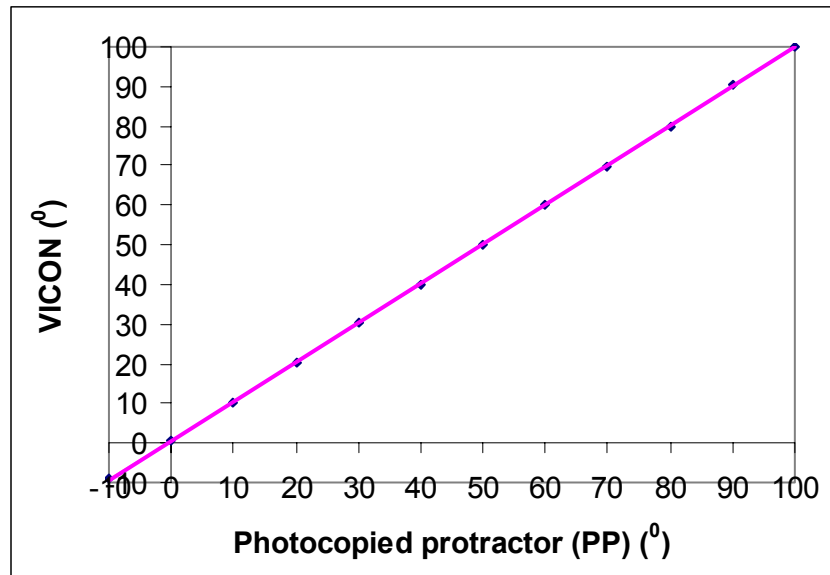
### **5.6.5.2 Methods**

The accuracy of angular measurement of the PP attached to the motorised device was established using the VICON camera system. The VICON camera system was calibrated (section 5.6.2.2) prior to data collection. The back of the PP was attached to a wooden board (120cm high and 30cm wide) with double-sided tape (Niceday, UK). Then reflective markers (2mm diameter) were attached to the PP (from  $-10^0$  to  $100^0$ , at  $10^0$  interval) using double-sided tape. The wooden board was erected using a tripod stand. Thereafter, the PP was captured with the reflective markers on it. The corresponding angles on the VICON and the PP were recorded. The agreement between the measurements obtained from the measuring instruments was examined using ICC and limits of agreement.

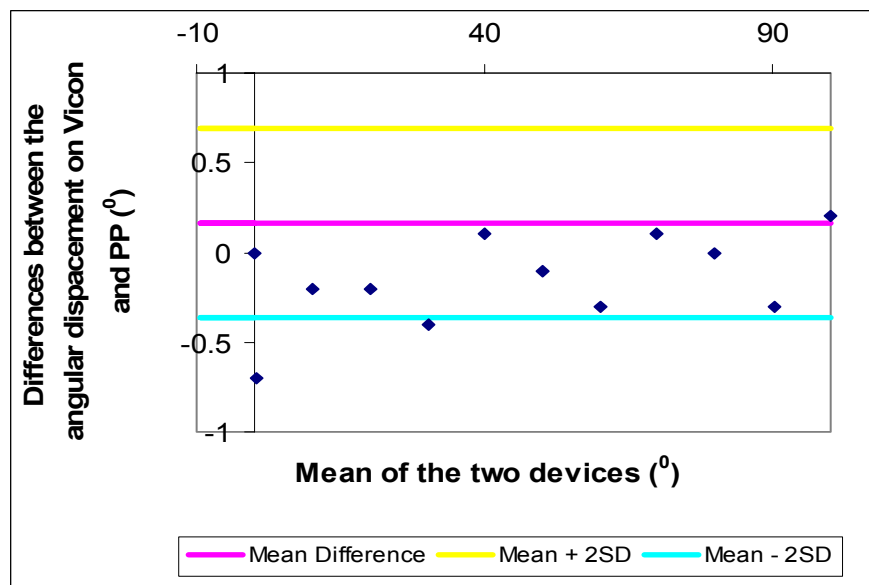
### **5.6.5.3 Results**

The angular measurements of the photocopied protractor and VICON are demonstrated in Figure 5.11. The Figure illustrates a linear relationship between these devices. Figure 5.12 shows the Bland and Altman plot of agreement between mean angular measurements of the two measuring tools and the difference between them. From Figure 5.12, the mean difference between the angular measurements obtained from both devices was small ( $-0.16^0$ ). Additionally, with the exception of two cases, the measured angles are within the 95% limits of agreement. Moreover, from the Figure (5.7b) 95% LOA reveal that zero lies between the 95% confidence interval ( $-0.69^0$  and  $0.36^0$ ) of the mean difference between the measuring devices. The angular measurements of the VICON system were sometimes higher than

those of the photocopied protractor. Furthermore a high ICC value (ICC = 0.97) was obtained between the measuring devices.



**Figure 5.11: Photocopied Protractor Plotted Against VICON.  $Y = a + bX$ ; where  $Y$  = predicted score,  $a$  = intercept constant and  $b$  = regression coefficient.**



**Figure 5.12 Bland and Altman Plot of Agree between the Mean and Angular Measurements of the Devices (PP and VICON) and their Differences**

#### **5.6.5.4 Discussion**

The results of this test showed an excellent agreement between the angular measurements obtained from the PP and VICON system. In addition, low systematic error existed between the measuring instruments. The findings of this experiment also revealed that a low random error was associated with the angular measurements using the photocopied protractor. There was a tendency that VICON cameras would systematically give higher readings than the photocopied protractor. The differences between these devices were small indicating good agreement between the angular measurements obtained from the two devices. However, given that 95% of the measured output was within  $-0.69^{\circ}$  and  $0.36^{\circ}$  this experiment suggests that angular measurements using the protractor are valid and accurate.

#### **5.6.5.5 Conclusion**

The results of this test demonstrated that angular measurement of the photocopied protractor was accurate. It appears that the photocopied protractor would be a useful device for angular measurements with minimal error. Consequently, a photocopied protractor was used by the researcher in the present study to measure angular displacement of the knee joint during proprioception testing in healthy children and children diagnosed with HMS.

### **5.6.6 Experiment 6: Criterion-related Validity of Healthy Subjects' Lower Leg Displacement Using the Motorised Device**

#### **5.6.6.1 Introduction**

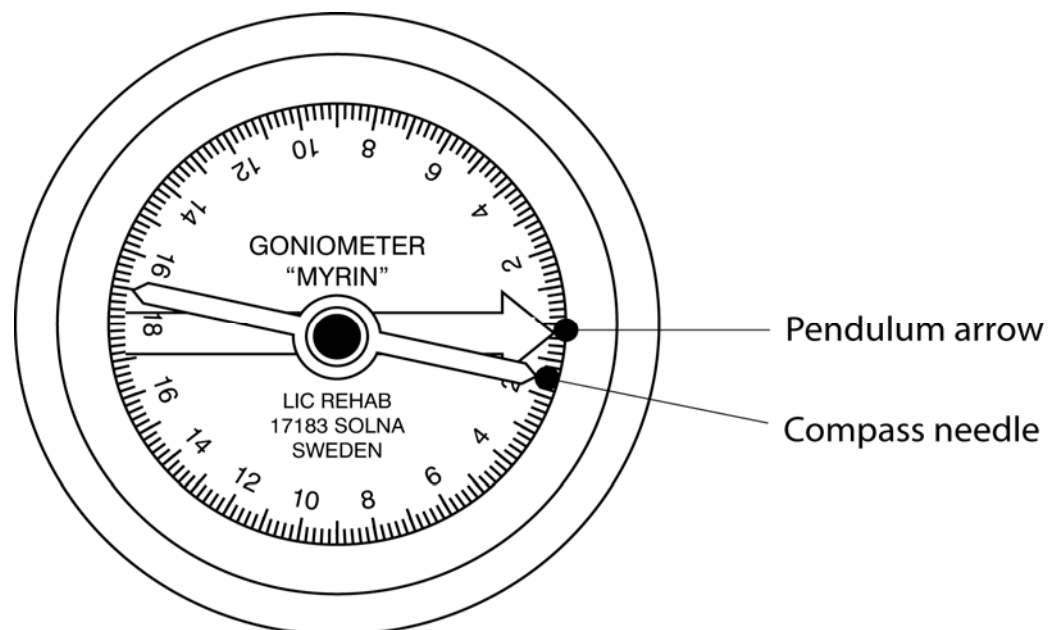
Only the study by Barrack et al. (1983c) investigated JK and JPS in children. Experiment 4 in section 5.6.4 of the thesis demonstrated an excellent accuracy of the angular displacement of the purpose built motorised device. Because the flexion-extension axis of the knee changes during knee movement (Snyder-Macker and Lewek 2006) it is difficult to maintain a correct alignment between the axis and the centre of rotation of the driving shaft of the device testing (Lehmkuhl and Smith 1983). Additionally, the examined knee joint may not produce a simple hinge-like movement. Consequently, displacement of the lower leg and that of the limb support attached to the motorised device may be different. This may lead to confounding results obtained during knee joint proprioception. The aim of this experiment was to investigate the criterion-related validity of the lower leg displacement on the purpose-built motorised device.



### 5.6.6.2 Methods

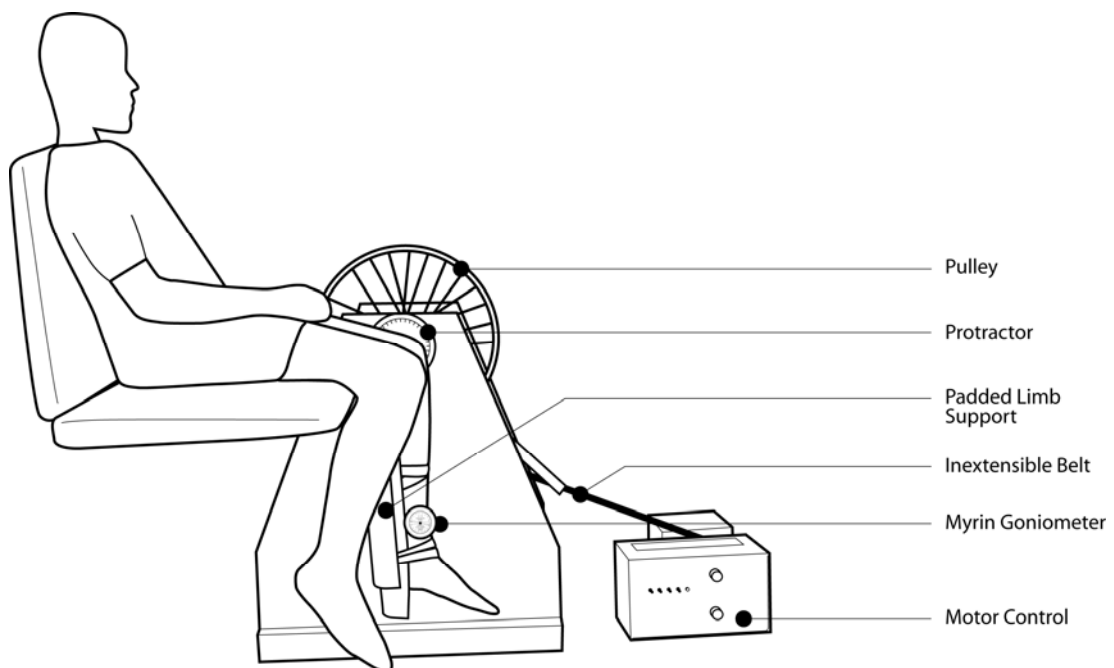
A convenience sample of 12 healthy subjects (6 adults and 6 children) participated in the experiment. None of the subjects had a history of knee injuries. The purpose and procedure of the study were explained to each participant. The study was approved by QMU, Edinburgh Ethics Committee and the Education Department of the City of Edinburgh Council. Informed written consent was obtained from all participants and parents of the participating children. Full details of recruitment are described in chapter 7 of this thesis.

To validate the motorised device as a measurement tool that can produce accurate lower leg displacement, a gravity dependent Myrin goniometer<sup>®</sup> (LIC Rehab, Sweden) (Figure 5.13) was used. The subject's test limb was determined in a randomised order using computer randomisation (SPSS). Each subject sat on an adjustable plinth with their lower leg placed in a padded support, while the centre of rotation of their knee joint (lateral femoral condyle) (Marks 1994; Xu et al. 2004) was carefully aligned with the centre of rotation of the driving shaft of the device (Marks 1994). The Myrin goniometer<sup>®</sup> (Figure 5.14) was then attached to the subject's lower leg just above the ankle (medial aspect of the test limb just above the medial malleolus) by means of a Velcro<sup>®</sup> strap (Angelopoulou et al. 1991). Subjects were instructed to relax and not move throughout the testing procedure.



**Figure 5.13: The Myrin Goniometer (illustration by Steve Kelly, Manchester Metropolitan University)**

The subject's knee was then passively moved into extension ( $0^{\circ}$  of knee extension) by the investigator using the motorised device. The Myrin goniometer<sup>®</sup> was reset to zero (before each measurement) such that the pendulum arrow coincided with the zero index mark (Tong 1983). The subjects' limb was then moved at a constant angular velocity of  $2.2^{\circ}/s$  to each of ten predetermined reference angles from  $0^{\circ}$  to  $90^{\circ}$  in a randomised order, and the value on the Myrin goniometer<sup>®</sup> corresponding to each lower leg displacement (angle) was recorded. The procedure was repeated three times and the mean value for each lower leg displacement measured by the Myrin goniometer was calculated. Angular velocities of  $10^{\circ}/s$  (Barrack et al. 1983a; 1983b; 1983c; Skinner et al. 1984; Friden et al. 1997) and  $3^{\circ}/s$  (Tsang and Hui-Chan 2003; 2004; Xu et al. 2004) have been used for knee JPS testing using motorised devices. The motorised device used in the present study had a maximum angular velocity of  $2.2^{\circ}/s$ . Therefore, subjects' limbs were moved by the motorised device at this angular velocity.



**Figure 5.14: Experimental set-up during validation test for lower leg displacement (illustration by Steve Kelly, Manchester Metropolitan University)**

Angles of 0° to 90° degrees were chosen because knee joint proprioception is usually tested within this range (Carter et al. 1994; Hurley et al. 1998; Selfe et al. 2006) and because they are within the functional range of motion (Bullock-Saxton et al. 2001). The Myrin goniometer® was used to validate the device because gravity dependent goniometers such as inclinometers (Garsden and Bullock-Saxton 1999) and Leighton Flexometer® (Thompson et al. 2003) have been used previously to assess knee JPS. Moreover, it was convenient for the participants. The VICON system was previously used by the researcher to validate the angular displacement of the motorised device under an unloaded condition (section 5.7.2). However, VICON was not used in this experiment because of the associated skin movement observed in a pilot experiment. The pilot experiment revealed that the experimental set up using VICON was inconvenient for the participants in terms of practical application. In addition, the experiment was time-consuming using the VICON. Moreover, unpublished results (Appendix 1) during the research revealed a high correlation between the Myrin and universal goniometers®. Data analysis was also carried out using ICC and 95% LOA (Rankin and Stokes 1998).

#### 5.6.6.3 Results

The characteristics of the participants are shown in Table 5.3. Lower leg displacement of the motorised device and Myrin goniometer® are demonstrated in Figure 5.15. Figure 5.16 shows the Bland and Altman plot of agreement between mean angular displacements of the two measuring tools and the difference between them. From Figure 5.16, it can be seen that the difference between the devices was small (0.24°) and within the 95% confidence interval. Additionally, from this Figure (5.15) 95% LOA revealed that 95% confidence interval of the difference between the devices ranged from -0.32 to 0.80. A high ICC value (ICC = 1.00) was obtained between the measuring devices.

**Table 5.3: Characteristics of the subjects (n = 12; 6 adults and 6 children)**

	<b>Age (years)</b>	<b>Body weight (kg)</b>	<b>Height (cm)</b>
Mean	19.1	59.3	156.8
SD	8.4	18.5	15.1
Range	8 - 30	27 - 9	130 - 173

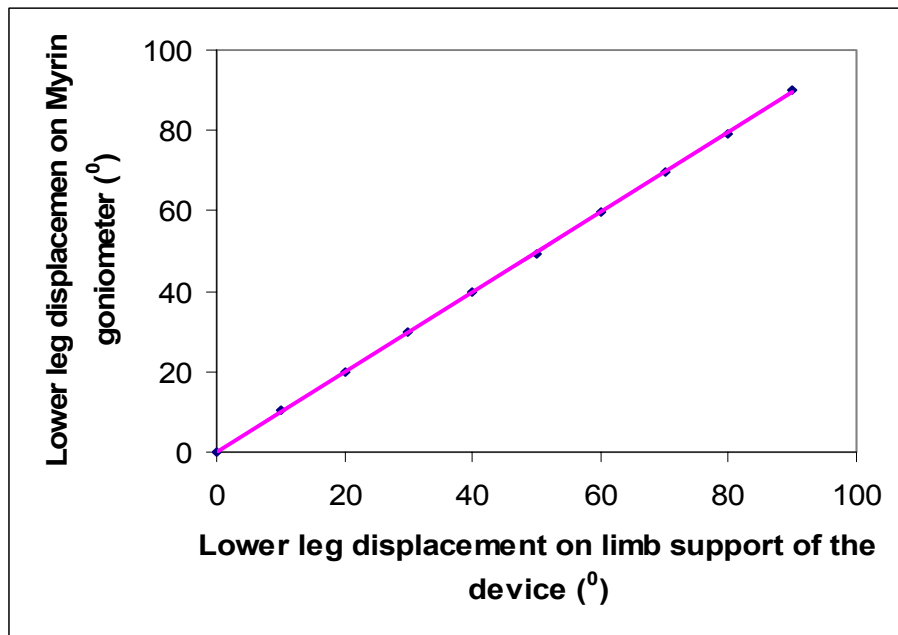


Figure 5.15: Lower leg displacement on motorised device plotted against Myrin goniometer.  $Y = a + bX$ ; where  $Y$  = predicted score,  $a$  = intercept constant and  $b$  = regression coefficient.

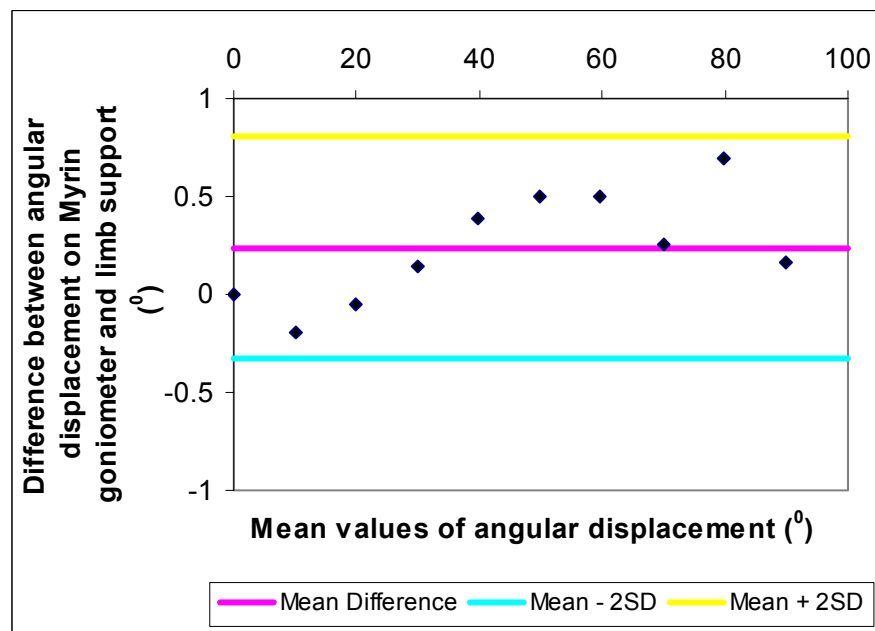


Figure 5.16: Bland and Altman plot of agreement showing the mean lower leg angular displacement and differences between the two measuring devices

#### **5.6.6.4 Discussion**

LOA revealed that the mean difference between the lower angular displacement on the Myrin goniometer<sup>®</sup> and that measured by the motorised device was around zero and within the 95% confidence interval. This suggests that there was no systematic change in the mean lower limb angular displacement measured by the measuring instruments. The range of LOA was small and implies that there was a low random error in the lower limb angular displacement measured by the Myrin goniometer<sup>®</sup> and the motorised device. The results therefore revealed an excellent agreement between the angular displacements measured by the instruments. Since 95% LOA of the difference in measured output were within  $0.24^{\circ}$ , indicating minimal variation, the motorised device appeared to be measuring the same variable as the Myrin goniometer<sup>®</sup>.

In the present experiment, a mean difference of  $0.24^{\circ}$  was recorded between lower leg angular displacement on the device and the Myrin goniometer<sup>®</sup>. Additionally, the 95% limits of agreement obtained in the previous experiment (section 5.6.4) ranged from  $-2.04^{\circ}$  and  $1.37^{\circ}$  and it ranged from  $-0.32^{\circ}$  to  $0.80^{\circ}$  in the present experiment. Moreover a high ICC value (ICC range = 0.96 to 1.00) was observed in the two experiments. These findings show that lower leg displacement and the movement of the limb support are in agreement indicating that the knee joint was properly aligned with the driving shaft of the device during movement. Based on these findings, it can be suggested that the angular displacement of the knee joint may not be different from that of the limb support of the device. However, this is just a presumption as the subjects' thighs were not strapped to the plinth during limb movement. This could have resulted in movement at the hip joint that may have affected the angular displacement at the knee joint.

#### **5.6.6.5 Conclusion**

The results of this investigation demonstrated that lower leg angular displacement of the motorised device is valid. Given the findings of this investigation, it seems that the purpose-built motorised device can be used to produce lower leg displacement accurately, with very minimal systematic and random errors. One potential limitation of the present experiment is that the lower leg displacement at the knee joint might have been affected by hip movement. Future study should be carried out to investigate the angular displacement of the knee joint on the device using two Myrin goniometers (one on the thigh to measure hip movement and the other above the

ankle for measuring knee joint angle) or a more sensitive measurement tool. Despite this limitation, the device was used by the researcher for assessing knee joint proprioception. Consequently, the between-trials repeatability of knee JPS assessment in healthy children was investigated using motorised device. The detailed account of the investigation is given in the following section.

### **5.6.7 Experiment 7: Between-trials Repeatability of Knee Joint Position Sense (JPS) Assessment in Healthy Subjects Using the Motorised Device**

#### **5.6.7.1 Background**

The previous section demonstrated excellent accuracy and criterion-related validity of angular displacement of the motorised device. Hence the device may be a useful instrument for assessing knee joint proprioception in children and patients with impaired muscle contraction affecting their examined limb. To determine the clinical utility of the device the between-trials repeatability of the device needed to be assessed.

At present, there is no standardised method of assessing knee JPS. Selfe et al. (2006) investigated the effect of number of trials during JPS in adults with patelofemoral syndrome using a dynamometer and recommended that five to six trials were needed before JPS data stabilised. To date, learning effects in healthy subjects during JPS assessment using motorised device have not been investigated. Studies of JPS with motorised devices by Barrack et al. (1983c), Skinner et al. (1984) and Corrigan et al. (1992) made no reference to practice trials before their test trials. On the other hand, authors like Friden et al. (1997) administered three practice trials, although they did not explain how they arrived at this number of trials. Similarly Grob et al. (2002) gave practice trials before the actual test trials but they did not indicate the number of trials administered. It is unknown whether there will be a change in absolute angular error (AAE) across a series of test trials following a set of practice trials at the same test angles. Hence, the aim of this experiment was to investigate the between-trials repeatability of healthy subjects during knee JPS assessment using a motorised device.

### **5.6.7.2 Methods**

Ethical approval was obtained from QMU ethics committee. 10 subjects (age range 7-31 years, 5 adults and 5 children) were recruited from the student population and children of staff at QMU. Informed written consent was obtained from all the participants. Parents of the participating children also consented to their children participating in the study. The purpose-built motorised device was used to assess JPS. Each subject received verbal explanation of the testing procedure. Subjects sat on an adjustable plinth with the test knee at 90° flexion. The knee joint axis (lateral femoral condyle) was aligned with the centre of rotation of the driving shaft of the device (Mark 1994; Xu et al. 2004) and the lower leg placed in the padded limb support attached to the motorised device.

The leg was passively moved by the device at a constant angular velocity of 2.2°/s to one of two different angles (25° and 10° knee flexion - the first angle tested was randomly selected). These angles were selected because they are believed to be within the working range of the knee during functional and weight-bearing activities (Barrett et al. 1991). Subjects were required to press a response button as soon as the target angle was sensed. To familiarise the participants with the test protocol, three practice trials, where the investigator stopped the device at the target angle, were performed with the subjects' eyes open. Subjects then closed their eyes and performed five test trials, pressing the response button themselves. Once one angle was tested, the process was repeated using the remaining angle. The absolute angular error (AAE) (the absolute difference between the target angle and the perceived angle) was calculated for each of the five trials for the two target angles for each subject. Due to the non-parametric nature of the data, statistical analysis was performed using Friedman tests and Wilcoxon signed-rank tests.

### **5.6.7.3 Results**

The characteristics of the participants are shown Table 5.4. Figure 5.17 shows the combined AAE for the two target angles. AAE for the two target angles in adults and children are illustrated in Figure 5.18 and 5.19 respectively. Significant differences were found between the 5 trials for both target angles in the combined group ( $p < 0.001$ ). Significant differences between the 5 trials were also found at both target angles in children (25°  $p = 0.022$ ; 10°  $p = 0.008$ ) and adults (25°  $p = 0.003$ ; 10°  $p = 0.001$ ), respectively. The summary of results of Friedman and Wilcoxon signed rank

tests are illustrated in Table 5.5. Appendix 4.1 illustrates the summary of the findings of this experiment, presented as a conference paper.

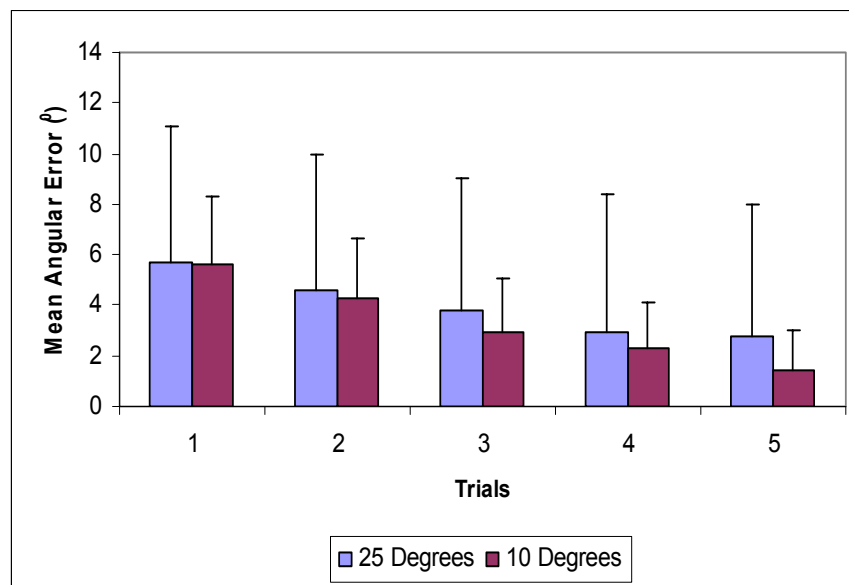
**Table 5.4: Physical characteristics of the subjects (n = 10; 5 adults and 5 children)**

	Age (years)	Height (cm)
Mean	19.1	158.2
SD	8.6	14.6
Range	7 -31	130 - 173

**Table 5.5: Results of Friedman's and Wilcoxon signed rank tests**

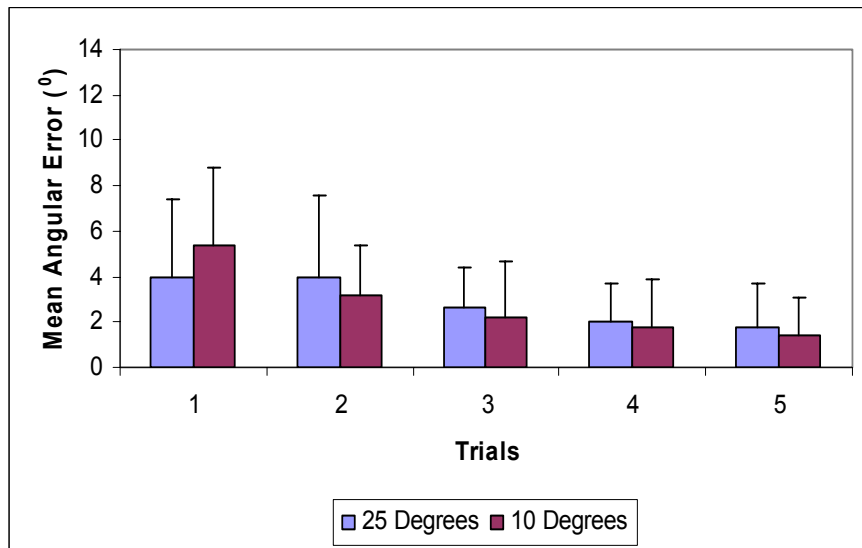
	Children (n = 5)		Adults (n = 5)		Combined (n = 10)	
	25°	10°	25°	10°	25°	10°
Overall	<b>0.022*</b>	<b>0.008*</b>	<b>0.003*</b>	<b>0.001*</b>	<b>&lt;0.001*</b>	<b>&lt;0.001*</b>
Trial 1 vs. 2	<b>0.006</b>	<b>0.026</b>	<b>0.039</b>	<b>0.043</b>	<b>0.041</b>	<b>0.039</b>
Trial 2 vs. 3	<b>0.020</b>	<b>0.016</b>	0.655	0.066	0.357	0.102
Trial 3 vs. 4	0.053	0.202	0.059	0.102	0.414	0.593
Trial 4 vs. 5	0.564	0.102	1.000	0.180	0.317	0.414

Significant p values are indicated in boldface, \* are Friedman's p values.

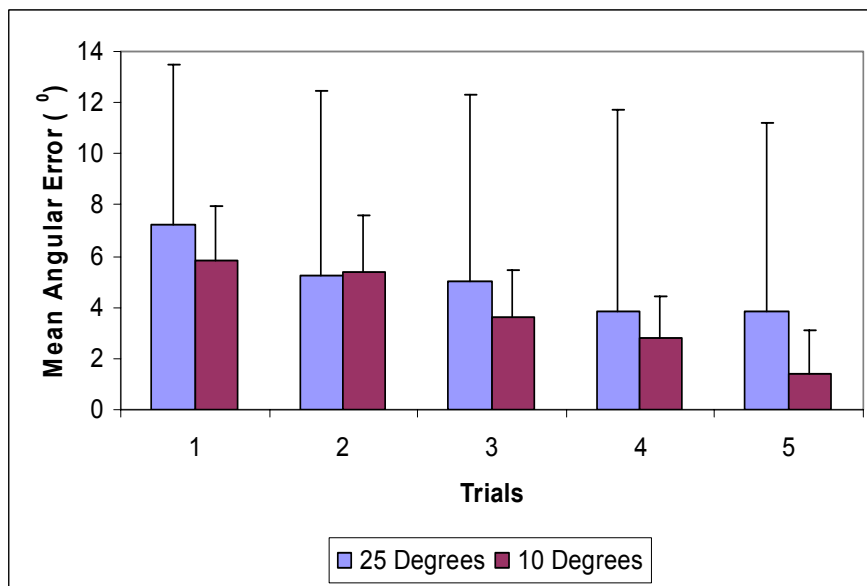


**Figure 5.17: Mean ( $\pm$  SD) absolute angular error at the two target angles in adults and children combined (n = 10)**





**Figure 5.18: Mean ( $\pm$  SD) absolute angular error at the two target angles in children (n = 5)**



**Figure 5.19: Mean ( $\pm$  SD) absolute angular error at the two targets angles in adults (n = 5)**

#### 5.6.7.4 Discussion

The between-trials repeatability study of JPS tests showed that absolute angular error (AAE) decreased from trial 1 to trial 5 at both target angles (both  $p < 0.001$ ). This suggests a possible learning effect taking place in healthy subjects during JPS assessment using the purpose-built motorised device. The same trend was also

observed when the study participants were grouped into adults ( $p < 0.001$ ) and children ( $p < 0.001$ ). There was no difference between trials 2 and 3 or later trials in the combined group suggesting that learning effects had stopped at the second trial. An alternative explanation for this observation may be that the present experiment was underpowered. No previous studies were found examining the between-trials repeatability of knee JPS test using a motorised device. The present findings are similar to those of Selfe et al. (2006). They found that passive knee JPS stabilised after five to six repetitions, using a dynamometer.

Marks (1994) reported a lack of within-session (two trials within a day) and between-sessions (3 sessions of 3 days interval) difference of active JPS tests in 16 healthy women (mean age 31.1 years). Garsden and Bullock-Saxton (1999) were unable to detect significant difference across six trials (within-session). They assessed active knee JPS in 20 patients with knee osteoarthritis and 20 aged-matched controls. Repeated measures analysis of variance showed that there was no trend across the repeated measurements of JPS at 20° and 40° knee flexion. It is believed that stabilisation is achieved more quickly during active than passive JPS test which may be due to greater level of peripheral afferent information generated during the active test compared to passive (Selfe et al. 2006). Therefore, the likely reason for these differences may be that active knee JPS was examined by Marks (1994) and Garsden and Bullock-Saxton (1999) while passive knee JPS was tested in the present study.

Additionally, the findings of the present investigation contrast with the observations of Ludon (2000) who investigated knee JPS at 10°, 30° and 60° in twenty-four women (aged 24 years) with genu recurvatum who participated in various exercise activities at least 3 times a week. Ludon (2000) examined within-session repeatability of JPS through a weight-bearing method and found that AAE increased across trials for the 30° and 60° target angles. However, no significant difference was found between trials at a target angle of 10°. Although the level of physical activity of the participants was not recorded in the present study, it is possible that the observed differences may be the result of the weight-bearing method and the level of physical activity of the subjects used, since exercise training has been found to improve joint proprioception (Aston-Miller et al. 2001; Ferrell et al. 2004). In addition, it is possible that the weight bearing method used in the study by Ludon

(2000) could also have led to muscle fatigue during repeated measurements of JPS and hence, the increased AAE.

The findings of the current investigation revealed that learning effects may be associated with JPS assessment in healthy subjects using a motorised device. The results of the present experiment imply that a quick one-off JPS assessment may not reveal individual's JPS acuity. This phenomenon therefore highlights the importance of adequate familiarisation of subjects to the test protocol during proprioception assessment. The learning effects observed in this experiment would be taken into consideration in the development of a protocol for knee joint proprioception assessment in this thesis.

#### **5.6.7.5 Conclusion**

AAE in healthy subjects during JPS testing using the device has been demonstrated to decrease across trials, suggesting that learning or memorisation effects occurred on the part of the participants. To minimise measurement error that may result from this phenomenon during knee JPS assessment, it might be necessary to administer three practice trials during knee JPS assessment. Moreover, at least two test trials may be required to demonstrate the actual proprioceptive ability in healthy children. The findings of this experiment were used for designing a detailed protocol of knee joint proprioception assessment for the clinical study in this research.

### **5.6.8 Between-days Repeatability of Reflective Marker Placement and Knee ROM during Walking in Healthy Subjects**

#### **5.6.8.1 Introduction**

The need for gait analysis in children diagnosed with HMS has been discussed in section 4.6. Moreover, the need for a quantitative gait analysis method such as the computer-aided video-based motion analysis system (VICON) has also been examined in section 5.7. The VICON motion analysis system is beginning to gain recognition as a valuable tool for gait disabilities assessment and for evaluating treatment. Light-weight body surface reflective markers are often used for computing joint angle motion (Kadaba et al. 1989). They are usually attached to specific anatomic landmarks. The validity of 3D gait analysis data depends on the ability of an investigator to place reflective markers correctly on these anatomical landmarks. It is also believed that skin movement may lead to significant error, which may result in variability in the data obtained (Schache et al. 2002). Hence, to obtain accurate

and valid knee motion during walking using the VICON system, accurate marker placement is of high importance. This experiment investigated the between-days repeatability of reflective marker placement and knee ROM during walking in healthy subjects.

#### **5.6.8.2 Methods**

Following ethical approval obtained from QMU, three healthy subjects (mean age  $14.3 \pm$  SD 15.4 years) participated in this experiment. Written informed consent was obtained from the participants (parents of the participating children also consented). The VICON camera system (Oxford Metrics, England) was calibrated (static and dynamic calibration) prior to data collection. Subjects had their weight, height, leg length, and width of both knees and ankles recorded.

Fifteen (14mm diameter) infra-red reflective markers were attached to the following anatomic locations as instructed by the VICON Clinical Manager manual (Van der Linden et al. 2002; Oxford Metrics, England 2004): the sacral marker was placed on the mid-point of the line connecting the two posterior superior iliac spines; bilateral pelvic markers on both anterior superior iliac spines; and thigh markers on the midpoint of the line connecting the greater trochanter and femoral condyle. Knee markers were placed on the lateral femoral condyles, shank markers were placed on the mid point of the line between the knee joint line and the lateral malleoli, and ankle markers on the lateral malleoli. Toe markers were placed between the second and third metatarsal head and heel markers on the calcaneum in vertical alignment with the toe markers.

Subjects were instructed to stand at the centre of the walkway where the static trial was captured. 3D gait data were collected while the subjects walked barefoot along a 7m long straight walkway at a comfortable speed. Each subject performed at least six trials (Kadaba et al. 1989; Oxford Metrics, England 2004). This procedure was repeated a week later. Both testing sessions were performed at the QMU HMAL. The agreement between the measurements obtained during the two sessions was examined using ICC and LOA (Rankin and Stoke 1998; Ageberg et al. 2007).

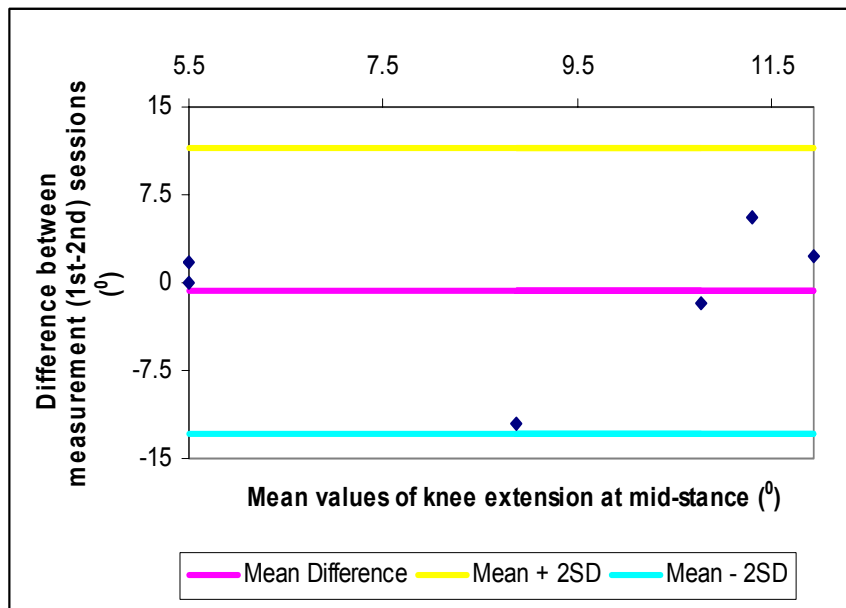
### 5.6.8.3 Results

The characteristics of the subjects are shown in Table 5.6. The Bland and Altman plot of agreement between knee kinematics' measurements obtained during the sessions is illustrated in Figures 5.20, 5.21 & 5.22. Figure 5.23 shows sagittal knee joint motion for both limbs during the two sessions. From Figure 5.20, it can be seen that the mean difference in knee extension in mid stance between the sessions was  $-0.69^{\circ}$ . 95% limits of agreement ranged from  $-12.80^{\circ}$  to  $11.53^{\circ}$ . A low ICC value of 0.07 was found between the repeated measurements of knee extension obtained during the two sessions.

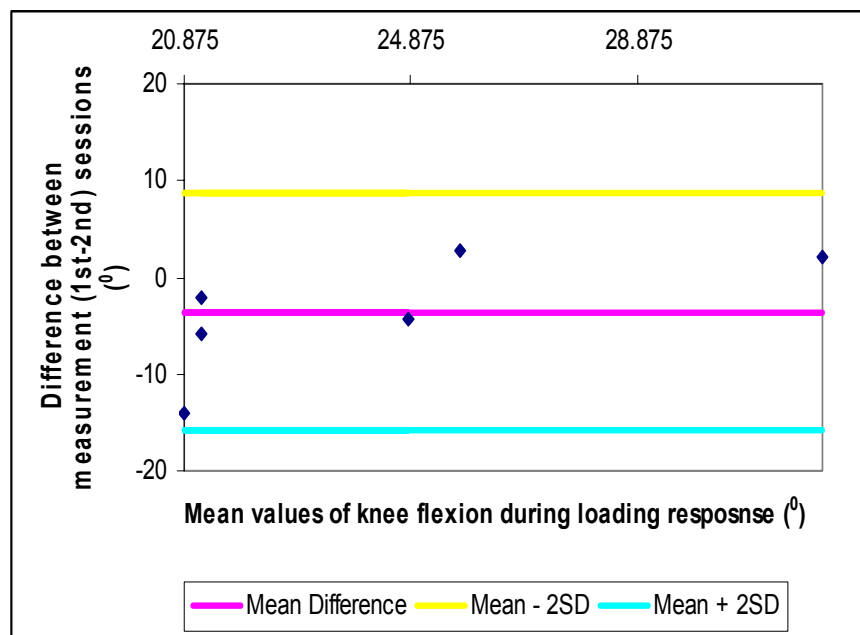
From Figure 5.21, the mean difference in knee flexion during the loading response between the two measurements was  $-3.54^{\circ}$ . Additionally, 95% limits of agreement show that zero lies between 95% confidence interval of the mean difference between the values obtained during the two sessions ( $-15.78^{\circ}$  to  $8.69^{\circ}$ ). This suggests that there was no significant systematic change between the repeated measurements. A low ICC value (0.34) was also obtained between the two measurements. Plot of agreement for maximum knee flexion obtained during the sessions is presented in Figure 5.22. The mean difference in maximum knee flexion during swing phase between the two measurement sessions was  $3.04^{\circ}$ . 95% LOA demonstrated that zero lies between 95% confidence interval ( $-15.55^{\circ}$  to  $21.63^{\circ}$ ). This also implies that there was no significant systematic change between the repeated measurements in swing phase. Furthermore, a low ICC value (0.11) was found between the measurement sessions. The mean knee angles obtained at each level of the gait cycle during the two sessions were similar (Figure 5.23). However, a wide range of confidence interval for the 95% LOA was demonstrated at these levels indicating that there was a high random error associated with repeated measurements of knee kinematic parameters.

**Table 5.6: Characteristics of the subjects (n = 3)**

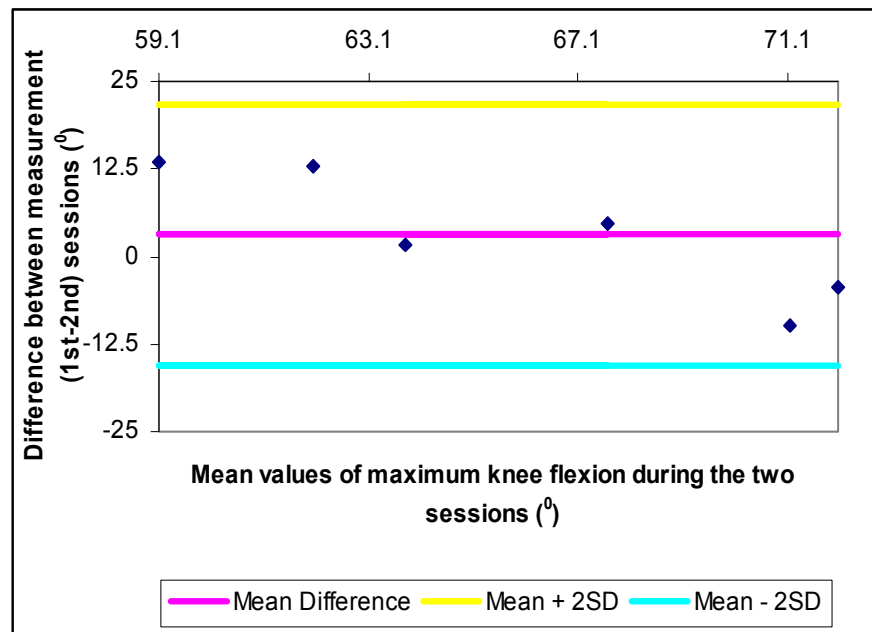
	<b>Age (years)</b>	<b>Weight (kg)</b>	<b>Height (cm)</b>
Mean	14.33	42.33	139.33
SD	15.37	8.74	25.01
Range	4 – 32	35 – 52	114 – 164



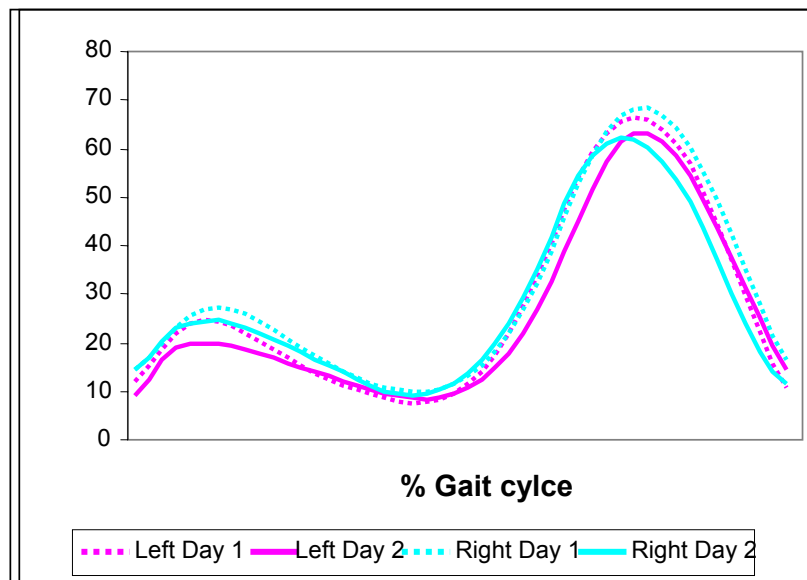
**Figure 5.20: Average values of knee extension during mid stance plotted against the differences between sessions**



**Figure 5.21: Average values of knee flexion during loading response plotted against the differences between sessions**



**Figure 5.22: Average values of maximum knee flexion during swing phase plotted against the differences between sessions**



**Figure 5.23: Sagittal knee motion in both limbs during the two sessions**

#### 5.6.8.4 Discussion

This investigation showed a low systematic and high random error in the three angular measurements using VICON system. Based on ICC, a poor agreement was observed between knee extension in mid stance, measurements of knee flexion during loading response, and maximum knee flexion between the two sessions. These findings further revealed that the between-days measurement of sagittal knee

motion may be associated with large variation when using VICON camera system. This variation may be due to inability of the investigator to consistently locate the knee joint axis of rotation. Additionally, it may also be the result of movement of the skin overlying the bony anatomical mark (Schache et al. 2002).

Furthermore, it appears that knee extension during walking may be underestimated by about  $13^{\circ}$  or overestimated by about  $12^{\circ}$  degrees. Knee flexion during loading response has the tendency of been underestimated by about  $-16^{\circ}$  or overestimated by  $9^{\circ}$ . Additionally maximum knee flexion may be undervalued by about 16 degrees or overvalued by about  $22^{\circ}$ .

#### **5.6.8.5 Conclusion**

The findings of this experiment demonstrated that between-days repeatability of reflective marker placement and knee ROM during walking might be associated with large random error, which may result in significant errors in the clinical use of VICON system. To minimise this variation in marker placement, a standardised protocol of marker placement procedure involving the use of a knee alignment device (KAD) for locating the knee joint axis may be required. Due to time constraints, repeatability experiment was not re-investigated to see if the KAD had the desired effect. However, the KAD was used to locate the knee joint axis during markers placement when examining the repeatability of the test protocol and in the clinical study in this research.

### **5.7 Overall Summary**

This chapter has provided a detailed account of the construction of the purpose-built motorised device for assessing knee joint proprioception. The accuracy and criterion-related validity of this instrument were examined. Additionally, the between-trials repeatability of JPS test using a motorised device was conducted in healthy subjects. Moreover, between-days repeatability of infrared marker placement and knee ROM during walking was also examined in healthy subjects. A high accuracy and criterion-related validity of the motorised device was demonstrated. However, the between-trials repeatability of JPS assessment varied across the trials. AAE decreased as trials increased in healthy subjects suggesting that learning effects occurred during the assessment. This phenomenon was taken into consideration in developing a protocol for knee proprioception assessment of children in this research. There was a large variation in the between-days repeatability of marker



placement and knee ROM during walking in healthy subjects. Therefore, knee alignment devices (KADs - one for each knee joint) were used to improve the accuracy of marker placement in this research, by determining the correct knee joint centre and joint axis alignment (Besier et al. 2001; Van der Linden et al. 2002).

The between-days repeatability of all the validated measurement tools including the VICON system and other outcome measures like the coloured analogue scale (CAS) and paediatric quality of life inventory (PedsQL) was determined in healthy children and children diagnosed with HMS. The test-retest of the outcome measures used in this study and intra-rater repeatability of the present researcher are reported in the following chapter.

## CHAPTER 6 : TEST- RETEST REPEATABILITY OF THE ASSESSMENT METHODS

### 6.1 Introduction

*Repeatability* is the extent to which an instrument can consistently measure the same parameter under specified conditions (O'Sullivan and Schmitz 2001). A repeatable instrument measures a phenomenon consistently, time after time, accurately, predictably, and without variation (O'Sullivan and Schmitz 2001). The terms *reliability*, *repeatability*, *reproducibility*, *consistency* and *stability* are often used interchangeably (Batterham and George 2000), however, to avoid confusion and for the purpose of uniformity; the term *repeatability* is used throughout in this thesis. Accurate assessment of clinical outcomes aid proper diagnosis as it helps to identify abnormality in children with pathological conditions such as hypermobility syndrome (HMS). It also enables the clinician to objectively determine progress or regression and to modify any treatment plans accordingly (Thibault et al. 1994). Repeatability is a component of validity. There are different types of repeatability. However, only those related to the present study i.e. test-retest and intra-rater are discussed below.

#### 6.1.1 Test-Retest Repeatability

Test-retest repeatability of an instrument is the consistency with which an instrument measures the same parameter repeatedly under the same conditions (Domholdt 2000). This is assessed by taking repeated measurements across the range of values expected to be found in actual use of the device (Domholdt 2000). Test-retest repeatability can be within-day or between-days.

**(a) Within-Day Repeatability:** Is when an instrument has a strong agreement during multiple measurement sessions taken on the same day and under specific conditions (Domholdt 2000).

**(b) Between-Days Repeatability:** This is when an instrument can consistently measure the same parameter under specific conditions on different days at the same time of day (Domholdt 2000).

### **6.1.2 Intra-Rater Repeatability**

Intra-rater repeatability is the consistency with which a researcher, therapist or practitioner measures the same parameter repeatedly under the same conditions (Domholdt 2000). Intra-rater repeatability is used to test whether the same researcher, therapist or practitioner using the same instrument comes to the same conclusions when presented with the same case on two or different occasions (Gomm et al. 2000).

Challenges to test-retest or intra-rater repeatability are a combination of random and systematic errors (Batterham and George 2000). According to these authors, random error refers to 'noise' in the measurement or test. Small random error in repeated measurements indicates a good repeatability. Systematic error as defined by Batterham and George (2000) is the non-random change between testing trials or sessions, where for example, all subjects perform consistently better in one trial than another. Random error results from several factors, including biological variation, causing a change in a person's ability between test and retest. Systematic error or bias may result from learning or fatigue effects during repeated testing (Batterham and George 2000; Ageberg et al. 2007).

Due to the developmental nature of the present work and to enhance generalisability of its findings it was necessary that the test-retest and intra-rater repeatability of the outcome measures be determined prior to use in healthy children and those with HMS. This chapter presents and discusses the test-retest (between-days) repeatability experiments conducted using a range of outcome measures in these children.

## **6.2 Repeatability of the Components of the Assessment Method**

### **6.2.1 Background**

Both neuromuscular impairments and quality of life (QoL) are integral parts of physiotherapy assessment in children with musculoskeletal complaints (O'Sullivan and Schmitz 2001). Physiotherapy research focuses on improvements in impairments such as (range of motion and muscle strength) in evaluating the efficacy of treatment (Jette 1993). On the other hand, it has been argued that the level of QoL in patients with musculoskeletal complaints may be affected (Bell et al. 1990). As a result of this, Bell et al. (1990) suggested that QoL measures be added to all clinical trials in rheumatology to complement the traditional anthropometric, clinical, and laboratory data. Furthermore, joint biomechanics, motor control, pain and proprioception are thought to be co-dependent, when considering the mechanisms, prevention and assessment of orthopaedic conditions (Baker et al. 2002).

The ultimate goal of providing physiotherapy services to patients with chronic disease is to alleviate their impairments, improve their functional status and overall QoL (Jette 1993). Presently, neuromusculoskeletal, functional ROM and QoL characteristics in children with HMS have not been well documented. Various methods have been used to identify these indices in children. In order for an assessment method to obtain widespread clinical acceptance as a useful clinical tool, the repeatability of its measurement is a fundamental requirement that must be sufficiently established (Brand and Crowninshield 1981). No studies were found examining the repeatability of any of the parameters included in the assessment methods in children with HMS. Neuromuscular performance, functional ROM during walking and QoL characteristics as well as the ability of physiotherapists to examine them may vary over time. Therefore, the aim of this study was to investigate the test-retest and intra-rater repeatability of such assessments in healthy children and those with HMS.

## **6.3 Methods**

### **6.3.1 Subjects**

Twenty children (10 healthy and 10 with HMS) aged 8 – 15 years participated in this investigation. The healthy group was recruited from local schools in Edinburgh and consisted of 5 boys and 5 girls. The HMS cohort was recruited from the Royal Hospital for Sick Children, Edinburgh and was made up of 2 boys and 8 girls diagnosed with HMS. None of the subjects enrolled in the study had history of trauma to either knee joint. No subject had visual impairment and none suffered from any systemic or vestibular-system disorders. Written informed consent was obtained from the participants and their parents/guardians before participation in the study. This study was approved by QMU Ethics Committee, the Education Department of the City of Edinburgh Council and the NHS Lothian Local Research Ethics committee. Participants were tested twice (one week apart) using the test protocol. This time interval was chosen because it was practically convenient for participants and their parents/guardians and to minimise possible learning effects on the part of the participants.

### **6.3.2 Testing Procedure**

Before testing, the investigator gave a brief explanation of the procedure to each subject, following which consent forms were signed by the participants and their parents/guardians. Then, subjects were asked to change into short trousers and their physical characteristics were assessed. Height was measured using a standiometer and body mass with a weighing scale. Leg length was determined in supine as the distance between the most prominent points of the anterior superior iliac spine (ASIS) to the most prominent point of the ipsilateral medial malleolus using a measuring tape (Wiggin et al. 2006). The following measurements were carried out according to the VICON Clinical Manager manual (Van der Linden et al. 2002): Knee width was assessed from distance between the lateral and medial femoral condyles in a standing position and ankle width was determined from the transmalleolar distance in standing, using an Anthrometer<sup>®</sup>. Lower limb dominance was also established as the leg used by the subject to kick a football (Sadeghi et al. 2000; Wiggin et al. 2006). Because exercise training may enhance joint proprioception (Petrella et al. 1997; Ashton-Miller et al. 2001; Roberts et al. 2004) and muscle torque (Faigenbaum et al. 1993; Morton et al. 2005), the level of physical activity was documented as the amount of time (hours) spent on sports and

or physical education per week (Engelbert et al. 2006). The test limb (knee) of the healthy children was determined using computer randomisation on SPSS. The more symptomatic (painful) knee of the HMS subjects was tested. Data for each subject's test knee was collected on the following six variables, in this order: QoL, pain, proprioception, muscle torque, PROM and functional ROM. To facilitate the testing set up and for the purpose of convenience on the part of the participants, the order of testing was not randomised. All measurements were carried out by a single rater (the researcher).

### **6.3.3 QoL Assessment**

QoL was assessed using the PedsQL™ (Varni et al. 2002) module 4.0 (UK English version) child (8-12 years) and adolescent self-report (13-18 years). Each participant was provided with a copy of the child or adolescent self-report questionnaire (Appendix 2a and b).

Teenagers were provided with a pen and a clipboard and were given the following instruction *"The PedsQL asks you questions about how you feel and what you think about your knee joint during the past 1 week. It is not a test, and there are no right or wrong answers. It takes about 5 minutes to complete. If you have any questions, please let me know. Please be sure you read the questions carefully and choose the response that is the closest to how you truly feel"*. The teenagers were given up to 10 minutes to complete the questionnaire. When they returned the completed PedsQL questionnaire, the investigator checked that each item was answered, and verified that no item had more than one response.

The investigator completed the questionnaire for the younger participants (8 – 12 years) by reading the questions and the possible answers to them. They were asked to choose one possible answer from the five possible responses. The investigator completed the questionnaire in this research because the first two children aged 8 - 12 years that presented for the study were not willing to complete the questionnaire by themselves. For ease of interpretation of PedsQL scores, items were reverse scored and linearly transformed from 0 - 4 to a 0 - 100 scale (i.e. 0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0) such that higher scores indicate better QoL (Varni 2006).

### 6.3.4 Pain Assessment

The average knee joint pain felt by the children over the last one week was assessed using a coloured analogue scale (CAS) (Figure 6.1). Each subject was shown the CAS with the slide marker at the middle of the scale (corresponding to 5 on the numeric scale). Then, a brief description of the CAS and how to use it was given to the subject by the examiner. *“This scale is like a ruler. The bottom, where it is small and there is hardly any colour at all means no pain at all. The top, where it is large, with deep red and a long way from the bottom means the most pain. I want you to slide the marker up or down the scale to show me how much pain you have in your knee within the last week”*. Once a child slid the marker to indicate the level of his/her pain, the examiner then turned the scale over and the corresponding number on the numeric scale was recorded (to the nearest whole number) as the subject's pain intensity.

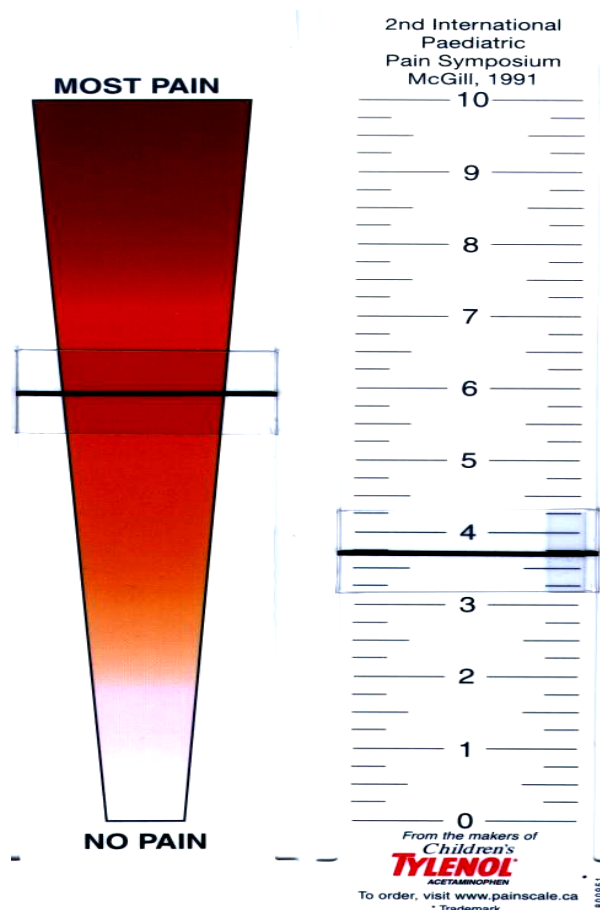


Figure 6.1: The Coloured Analogue Scale

The CAS manufacturer recommended that the slide marker should be positioned at the bottom of the scale. However, the marker was positioned at the middle of the scale in this research because the researcher felt that positioning the slide marker at the bottom of the scale might influence a child's judgement as a child may want to please the researcher by moving the slide up the scale even when the child was not experiencing pain.

### **6.3.5 Joint Proprioception Assessment**

Joint proprioception was tested in two ways. The first method was a kinaesthetic sense test joint kinaesthesia (JK) which consisted of determining the threshold for perception of movement when the angle of the joint was altered slowly (less than half a degree per second) (Corrigan et al. 1992). The second method was a joint position sense test (JPS). This examined the ability of a subject to reproduce an angle at which the joint had previously been placed (Corrigan et al. 1992). The two tests were chosen because studies have demonstrated a lack of significant correlation between knee JK and JPS tests (Grob et al. 2002; Friden et al. 1997). Therefore, it is possible that each test assesses different facets of proprioception and either one of the tests may not determine the overall proprioceptive impairment.

These tests were carried out with the purpose-built slow speed motorised device. The two methods used were modifications of those described by Barrack et al. (1983abc), Corrigan et al. (1992) and Grob et al. (2002). The motorised device moves the lower leg at a slow and constant angular velocity (corresponding to  $0.08^{\circ}/s - 2.2^{\circ}/s$ ). Detailed description of the device has been provided in section 5.3. JPS was tested at two target angles ( $25^{\circ}$  and  $10^{\circ}$  of knee flexion). These test angles were chosen because it is believed that joint receptors respond mainly near the end positions of joints (Gandevia and Burke 1992; Borsa et al. 1997) and HMS subjects may lack the ability to control the end-range of extension in the lax joints (Hall et al. 1995). Moreover, these angles were within the working range of the knee during functional and weight-bearing activities (Barrett et al. 1991). Additionally, these angles were chosen for the purpose of participants' safety. A pilot study in healthy children revealed that some subjects had the tendency of overestimating the test angle, in an attempt to reproduce the joint angle for the  $10^{\circ}$  knee flexion trial. Therefore, a test angle nearer to full extension of the knee joint (< than 10 degrees of knee flexion) may predispose to joint damage if subjects were unable to reproduce the test angle correctly. Furthermore, because knee extension deficit may



be seen in some individuals, the most extreme joint positions were excluded to avoid variable tissue tensions in participants and to allow them to relax without having their leg forced into maximum extension (Ageberg et al. 2005; 2007).

#### **6.3.5.1 Joint Kinaesthesia (JK)**

Kinaesthesia (threshold to detection of passive movement) was assessed with the participants in high sitting on an adjustable plinth with the back supported and reclined to  $60^{\circ}$  to encourage relaxation. Each participant sat with his/her legs hanging freely over the edge of the chair 4 – 6 cm proximal to the popliteal fossa such that the knee joint was not in contact with the edge of the plinth (Xu et al. 2004). This ensured that the participant's cutaneous sensation was minimised. Then the centre of rotation of the test knee joint (lateral condyle of femur) was aligned with the centre of rotation of the driving shaft of the device so that the angular displacement of the knee joint was equal to that of the frame attached to the limb support (Beynnon et al. 2000; Xu et al. 2003). The test limb was then placed in a padded limb support attached to the device. The starting position of the test knee and the aluminium frame of the limb support were maintained at  $60^{\circ}$  of knee flexion (Skinner et al. 1984; Skinner et al. 1986; Grob et al. 2002). To ensure that the same starting position was maintained for each subject, Velcro® straps were used to strap the test limb to the limb support as suggested by Skinner et al. (1984).

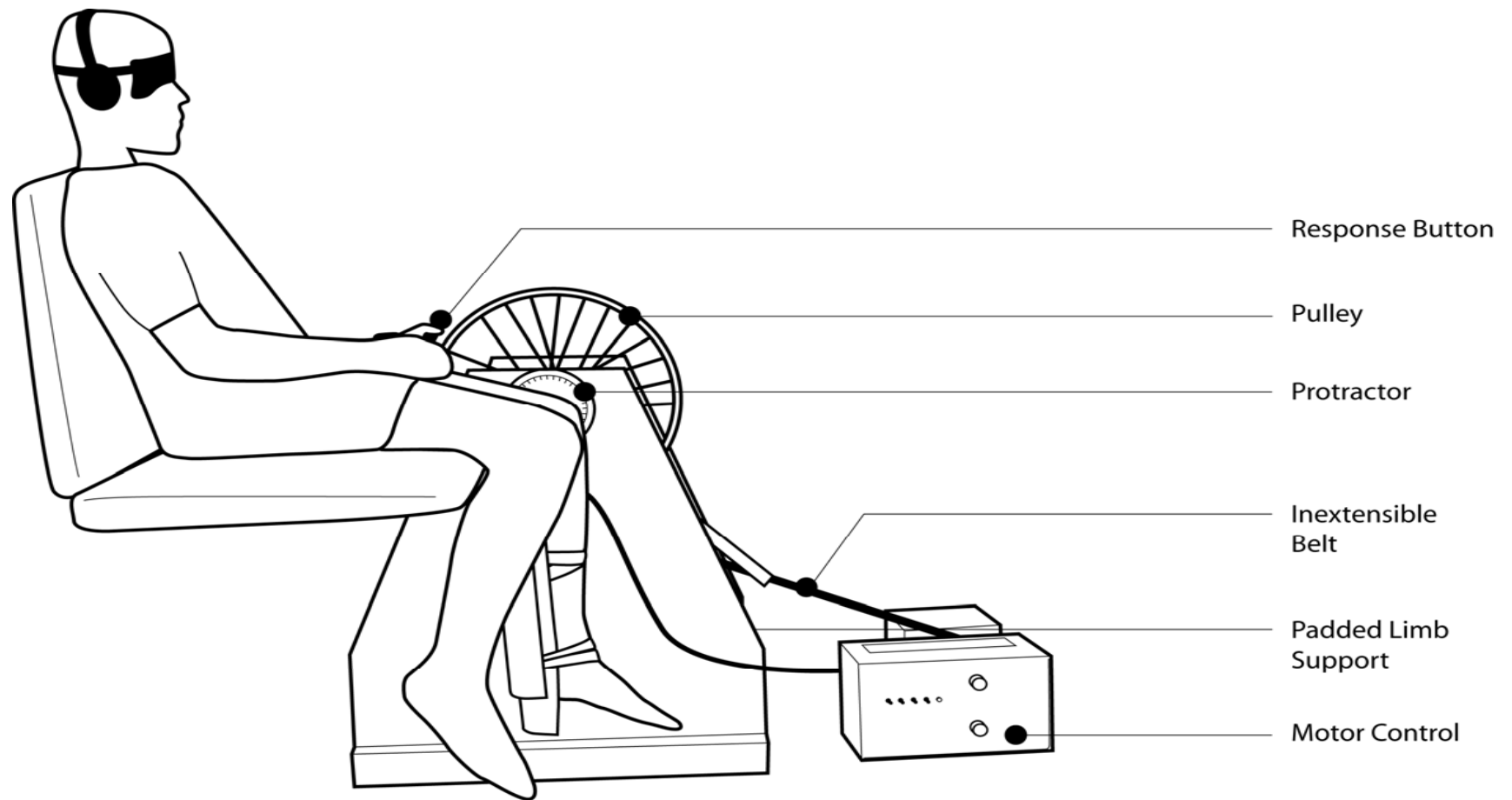
Three practice trials were performed by each subject to ensure that they understood the instruction given by the examiner and were familiar with the test procedure. During this period, the researcher was responsible for stopping the device using the response button once there was a change in knee joint position. The subject was then given the response button and was told that the motor would be started, and the test limb would move into extension slowly after a random delay of 5 to 15 seconds (Friden et al. 1997; Ageberg et al. 2005; Ageberg et al. 2007). A random delay was used so that the participants were not able to detect the movement of their limbs using the sound of the motorised device. A pulley was made to drive the wheel attached to the aluminium frame at a constant angular velocity of  $0.38^{\circ}/s$ . This angular velocity was used as it was the closest to those ( $0.4 - 0.5^{\circ}/s$ ) used to test JK (Xu et al. 2003; Ferrell et al. 2004; Friden et al. 1997; Ageberg et al. 2005; Ageberg et al. 2007). The participant was instructed to press the response button once they detected position change in the test limb. This immediately stopped the

movement. After each test trial, the examiner asked the participant to confirm if they were sure that the test limb actually moved. In a case where a participant pressed the switch before movement of the test limb occurred, the trial was repeated. To minimise visual and auditory sensory input the participants were blindfolded and they wore earmuffs during the practice and test trials. The angular displacement of the knee joint for the second test trial (before the subject detects position change) was read from the protractor attached to the device and recorded as the threshold response for the subject. Evidence suggests that five to six repetitions were needed before passive JPS data stabilised in adults with patelofemoral pain syndrome (Selfe et al. 2006). A pilot study carried out by the present researcher in healthy adults and children (section 5.6.7) revealed that learning effects occurred during JPS tests and this phenomenon stopped after the second test trial and therefore the second trial was used for data analysis. However, to ensure that legitimate data was collected from each participant, three test trials were carried out. The same number of practice and test trials was administered for both proprioception outcome measures, to standardise the test procedure.

#### **6.3.5.2 Joint Position Sense (JPS)**

The experimental set up and participants' positions were similar to the above section, except that the starting position of the test knee joint was  $90^0$  (Barrack et al. 1983a; Skinner et al. 1984; Beynnon et al. 1999; Grob et al. 2002; Sekir and Gur 2005). The plinth was adjusted such that the knee axis of rotation (lateral femoral condyle) corresponded to the centre axis of the shaft (Figure 6.2) (Marks 1994; Macdonald et al. 1996; Tsang and Hui-Chan 2003; Tsang and Hui-Chan 2004; Xu et al. 2004). As with the JK test, external cues (visual and auditory) to the test limb position or motion were also minimised so that only the receptors emanating from the knee joint and the surrounding tissues were activated during the testing (Skinner et al. 1986; MacDonald et al. 1996). A starting position of  $90^0$  was chosen because for movement about the knee, the current view seems to be that most joint receptors remain quiet through out the middle ranges of motion (Johansson et al. 1991). This was done so that the joint receptors would not be fully activated until the joint had been moved to the target position. In addition, this starting position has been used previously to test knee JPS (Barrack et al. 1983b; Skinner 1986; Grob et al. 2002; Hassan et al. 2002; Sekir and Gur 2005) and therefore there findings were available for comparison.

The motorised device then moved the participant's test limb at an angular velocity of  $2.2^{\circ}/\text{s}$  from the starting position ( $90^{\circ}$  of knee flexion) to two pre-determined test angles of  $25^{\circ}$  flexion and  $10^{\circ}$  flexion. To enable the subject to remember the test positions, the test limb was held in these positions for approximately 10 seconds (Callaghan et al. 2002) and subjects were asked to concentrate on the position. The leg was then returned to the starting position using the motor, where it was left for 15 seconds (Corrigan et al. 1992). A pilot experiment (section 5.12) demonstrated that it took the proprioception device approximately 30s and 36s to move subjects limbs from the starting position to the test angles of  $25^{\circ}$  and  $10^{\circ}$  respectively.



**Figure 6.2: Experimental set-up for the knee JPS testing (illustration by Steve Kelly, Manchester Metropolitan University)**

To familiarise the subjects with the test procedure and to allow learning effects to take place, the procedure was practiced 3 times for each test angle. Subjects were also blindfolded and they wore earmuffs during the practise and test trials (Figure 6.2). Due to the reasons already discussed in section 5.2, an air splint was not used to minimise cutaneous sensation in present study. In addition, it is believed that cutaneous sensation has an insignificant role in JPS of a proximal joint (Grigg 1994) such as the knee. Moreover, knee JPS has been tested previously without the use of an air splint (Dvir et al. 1988; Marks 1994; Birmingham et al. 1998).

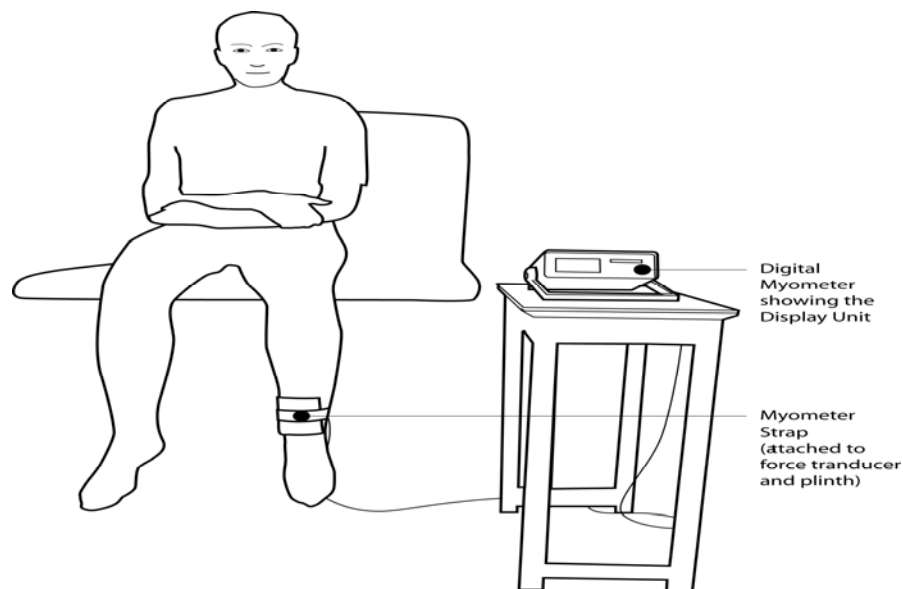
Each subject was instructed to relax and not to assist the movement voluntarily during the testing so that no muscular contraction took place (Callaghan et al. 2002; Selfe et al. 2006). The present researcher cannot say for sure whether the participants were fully relaxed or not as this was not examined objectively (the use of EMG for this purpose has already been discussed). Subjects were told to press the response button when they thought that the test limb had been placed in the test position previously demonstrated. A slow speed of  $2.2^{\circ}/s$  was chosen to minimise the tendency for the subjects to deduce the test position based on movement cues (Lonn et al. 2000) and to limit reflexive muscle contractions (Callaghan et al. 2002). Moreover, it is believed that slow and constant angular velocity maximally stimulates joint proprioceptors (Friden et al. 1996; Ageberg et al. 2005; 2007) and minimises the contribution from muscle receptors (Ageberg et al. 2005; 2007) by limiting reflexive muscle contraction (Callaghan et al. 2002; Selfe et al. 2006). In addition, the device used for this study has a maximum angular velocity of  $2.2^{\circ}/s$  which is similar to that used ( $2^{\circ}/s$ ) in the studies of Callaghan et al. (2002) and Selfe et al. (2006). The angular displacement for each trial at each target angle was recorded. The absolute angular error (AAE) for the second test trial at each target angle (absolute difference between the target and perceived angles) was calculated and was used for data analysis.

### 6.3.6 Muscle Torque

The peak isometric torque (Nm) of the knee extensors and flexors was quantified using the digital myometer (MIE Ltd, Leeds, England).

#### 6.3.6.1 Knee Extensors

Subjects sat on a plinth with the test knee flexed to  $90^{\circ}$ . The starting position of  $90^{\circ}$  was chosen because it is believed that the optimal angle of quadriceps muscle pull occurs when the muscle is pulling at a  $90^{\circ}$  or perpendicular to the bony segment (Clarkson 2000). A non-extensible myometer strap was strapped around the lower leg 5cm proximal to the base of the malleoli of the subjects' test limb and the other end was attached to the myometer transducer. 5 cm was chosen to standardise the position of the strap. Another non-extensible strap was attached to the frame of the couch (underneath) and to the other end of the myometer transducer (Figure 6.3).



**Figure 6.3: Experimental set-up for knee extensor muscle torque testing (illustration by Steve Kelly, Manchester Metropolitan University)**

The perpendicular distance (m) between the lateral knee axis of rotation and the myometer strap (moment arm) was measured with a tape and recorded. Participants were asked to try to straighten their knees from the starting position ( $90^{\circ}$ ). *"I would like you to straighten your knee as much as you can"*. Participants were given consistent verbal instruction and encouragement. The maximum force (N) produced by the extensors displayed on the myometer was recorded. To calculate the torque

value generated by the quadriceps, the force produced by the extensors was multiplied by the moment arm (Smidt and Rogers 1982; Effgen and Brown 1992) and recorded as extensor muscle torque for each subject.

#### **6.3.6.2 Knee Flexors**

Similarly, knee flexor muscle torque was measured with the participants in the same starting position and the same experimental set-up and procedure except that the myometer was placed on the posterior aspect of the lower leg. Participants were also given consistent verbal instruction and encouragement "*I would like you to bend your knee as much as you can*", the maximum force produced by the hamstrings displayed on the myometer was also recorded. Then, flexor muscle torque was calculated for each subject. To prevent extensor and or flexor muscle fatigue, only one trial was carried out by the participants. To account for the influence of body mass on muscle torque, both extensor and flexor muscle torque were normalised to body mass (Keating and Matyas 1992).

#### **6.3.7 Passive Range of Motion (PROM)**

The participants' PROM was determined using a universal goniometer (Jamar, USA). Subjects lay supine on a couch with their knee in extension. A rolled towel was and placed under the ankle of the test limb, to ensure that the knee joint was at zero degrees (Reese and Brandy 2002). PROM as opposed to active was chosen to prevent limitation of ROM that may be associated with pain and muscle weakness as may be the case in children with HMS (Robin and Everman 1998). Moreover, young children may be unwilling to perform full active range of motion (Reese and Brandy 2002). Supine was chosen because it is believed that knee flexion may be limited in prone due to tightness of the rectus femoris muscle (Reese and Brandy 2002).

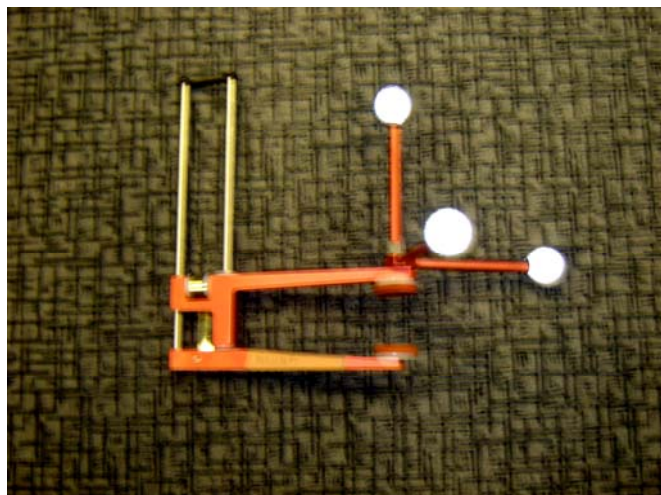
Subjects were asked to relax during the testing. With subjects in this position, the centre of the universal goniometer was aligned with the lateral femoral condyle; the moveable arm with the lateral malleolus; while the immovable arm was aligned with the greater trochanter (Gogia et al. 1987; Reese and Brandy 2002). The participant's knee joint was passively extended by the examiner through its pain free ROM and the reading on the universal goniometer was recorded. The knee was then returned to its original starting position by the examiner. Similarly, knee flexion of the subjects was measured by the examiner passively flexing the knee joint

through its available range. The goniometer reading was then recorded as knee flexion PROM.

### **6.3.8 Functional ROM**

Knee joint motion in a sagittal plane was assessed using the VICON 3-D motion analysis system (VICON 612, Oxford Metrics Ltd., Oxford, England). Eight M8 VICON cameras (Oxford Metrics Ltd, Oxford, England) were used, operating at a 100 Hz sampling rate, mounted on the wall (3m high), positioned at right angles and approximately 3m away from a 7m walkway. The cameras were connected to a data station, which was in turn connected to a computer.

The procedure for gait analysis was similar to the one described in section 5.6.8 except for the use of knee alignment devices. Participants were requested to stand (Oxford Metrics Ltd, Oxford, England, 2004) at the centre of the walkway where the knee alignment devices (KADs) (Figure 6.4) (one for each knee) were placed on the knee joint axis (marked with pen). Then the static trial was captured with the KADs in place. Thereafter, KADs were removed and markers were placed on those points (both lateral femoral condyles) (Figures 6.5 and 6.6). The KADs were used to define the knee joint flexion-extension axis of rotation. Earlier investigation of the between-days repeatability of marker replacement and functional ROM measurements in the sagittal plane, in healthy subjects (section 5.6.8) showed poor repeatability (ICC range = -0.07 to 0.34).



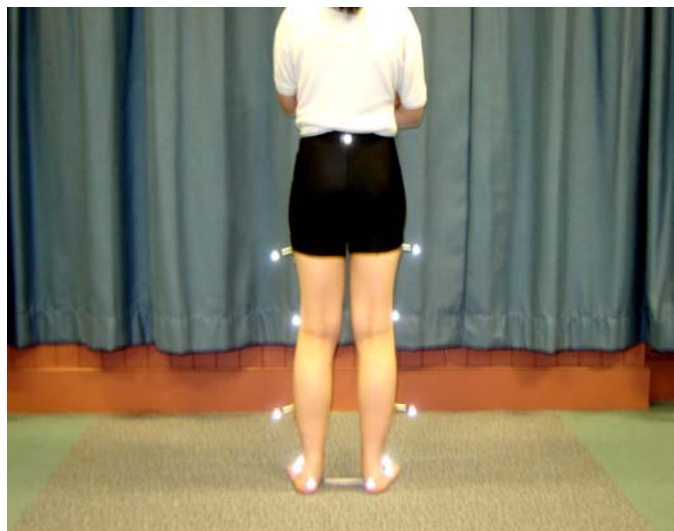
**Figure 6.4: Knee Alignment Device**





**Figure 6.5: Marker placement on a subject's anatomical landmarks (anterior view)**

Subjects were instructed to walk barefoot 6 times at a self-selected (*"I would like you to walk the way you normally walk"*) pace along the 7m level walkway. The first 2m allowed for acceleration and normal ambulation, the last 2m allowed for deceleration, and the middle 3m was used for data capturing. The average knee joint angles during the 6 walks normalised for one full gait cycle were calculated for each subject using the computer Polygon<sup>®</sup> software (Oxford Metrics Ltd, Oxford, England, 2004) and were used for data analysis.



**Figure 6.6: Marker placement on a subject's anatomical landmarks (posterior view)**

### **6.3.9 Data Analysis**

The repeatability of the data collected during the two sessions in healthy children was analysed, except for pain. This was because a pain rating for all participants was zero during both sessions. The data obtained in children with HMS for all the measurement parameters were analysed. Two measures of repeatability were calculated for each group: Intraclass correlation coefficient (ICC) and 95% limits of agreement (Rankin and Stokes 1998; Potter et al. 2005). ICC has been used extensively for reporting the repeatability of clinical measurements and therefore allows comparison with other studies. Bland and Altman plots were generated to show the relationship between the differences in first and the second measurements (test 1 minus test 2) against their mean. In addition, 95% limits of agreement (mean difference between the two measurements  $\pm 1.96$ SDs) (Bland and Altman 1986) were calculated for all the outcome measures. ICC was also used to examine the repeatability of the combined group (set of data from both healthy children and those with HMS). ICC value was considered as poor when it was below 0.6, good between 0.6 and 0.8 and excellent when it was 0.8 and above (Merlini et al. 1992; Tiffreau et al. 2007).

## **6.4 Results**

### **6.4.1 Healthy and HMS Groups**

The characteristics of the healthy and the HMS subjects are shown in Table 6.1. The mean (SD)/median (IQR) of all measurements, ICC values, the mean difference between the two measurement sessions and the 95% limits of agreement between these sessions (1 and 2) in the two groups are summarised in Tables 6.2 and 6.3. Figures 6.7 to 6.29 illustrate the Bland and Altman plots of agreement between the mean of the two measurements for all the variables and the difference between the measurement sessions in the two cohorts. The mean knee joint angle measurements during walking in healthy children and HMS children are shown in Figures 6.30 and 6.31.

**Table 6.1: Characteristics of the healthy children (n = 10) and with HMS subjects (n = 10)**

	<b>Healthy Mean</b>	<b>Children SD</b>	<b>Children with HMS Mean</b>	<b>SD</b>
Age (years)	9.9	2.1	11.8	1.3
Height (cm)	143.9	16.9	150.2	18.6
Weight (kg)	43.6	16.1	48.1	21.2

95% limits of agreement (LOA) revealed an acceptable level of between-days variation for all the measurement variables in both groups, with the exception of the JPS tests. In addition, 95% LOA also showed that the between-days measurement error for knee extension in mid stance and maximum knee flexion during the swing phase in healthy children was high. Similarly, 95% LOA demonstrated that the between-days variation in knee extension in mid stance and knee flexion during loading response in the HMS cohort was large. Based on LOA, these findings suggest that all variables were assessed with high repeatability in both healthy children and those with HMS except for the JPS tests (at 25° and 10°) and knee extension in mid stance. Knee flexion during the loading response of walking and maximum knee flexion during swing phase were examined with low repeatability in the healthy children and HMS respectively.

The ICC values for all the measurement outcomes were high in the healthy children (range 0.82 - 0.98), with the exception of JPS measurements, knee extension in mid-stance and maximum knee flexion during swing (ICC range = 0.26 – 0.74). The ICC values of all measurement parameters in the HMS group were high (range 0.81 - 0.96) except for the JPS tests, knee extension in mid stance and knee flexion during loading response (ICC range = 0.18 – 0.68). The high ICC values recorded for some of the variables indicate excellent agreement between the two measurement sessions for these outcomes. On the other hand, the low ICC values obtained for some of the measurement parameters, suggest poor to good agreement between repeated measurements by the researcher.

**Table 6.2: Results of between-day repeatability in healthy children (n = 10):  
Mean (SD) or Median (IQR)**

Variable	Day 1	Day 2	ICC	Mean Difference	95% Limits of Agreement
Pain	0	0	-	-	-
*QoL	100.0 (2.50)	100.0 (0.00)	0.95	-1.96	-10.30 to 6.38
ROM Extension ( $^{\circ}$ )	-5.30 (2.06)	-5.10 (1.85)	0.95	0.2	-1.07 to 1.47
ROM Flexion ( $^{\circ}$ )	141.0 (2.91)	141.30 (2.79)	0.96	-0.3	-1.95 to 1.35
Muscle Torque Extensors (Nm/kg)	1.37 (0.24)	1.39 (0.25)	0.98	-0.02	-0.12 to 0.07
Muscle Torque Flexors (Nm/kg)	0.73 (0.18)	0.74 (0.17)	0.95	-0.01	-0.13 to 0.10
Kinaesthesia ( $^{\circ}$ )	2.00 (0.82)	2.10 (1.10)	0.83	-0.1	-1.24 to 1.04
JPS at 25 ( $^{\circ}$ )	4.00 (2.67)	2.60 (2.01)	0.39	1.4	-3.43 to 6.23
JPS at 10 ( $^{\circ}$ )	2.80 (3.26)	1.40 (1.08)	0.26	1.4	-4.27 to 7.07
Peak Knee Extension Mid Stance ( $^{\circ}$ )	4.71 (5.91)	3.92 (3.59)	0.74	1.27	-7.75 to 10.28
Knee Flexion During Loading Response ( $^{\circ}$ )	19.61 (9.43)	18.22 (6.32)	0.84	0.72	-6.15 to 7.59
Maximum Knee Flexion ( $^{\circ}$ )	61.89 (7.97)	59.41 (6.93)	0.48	2.26	-12.91 to 17.42

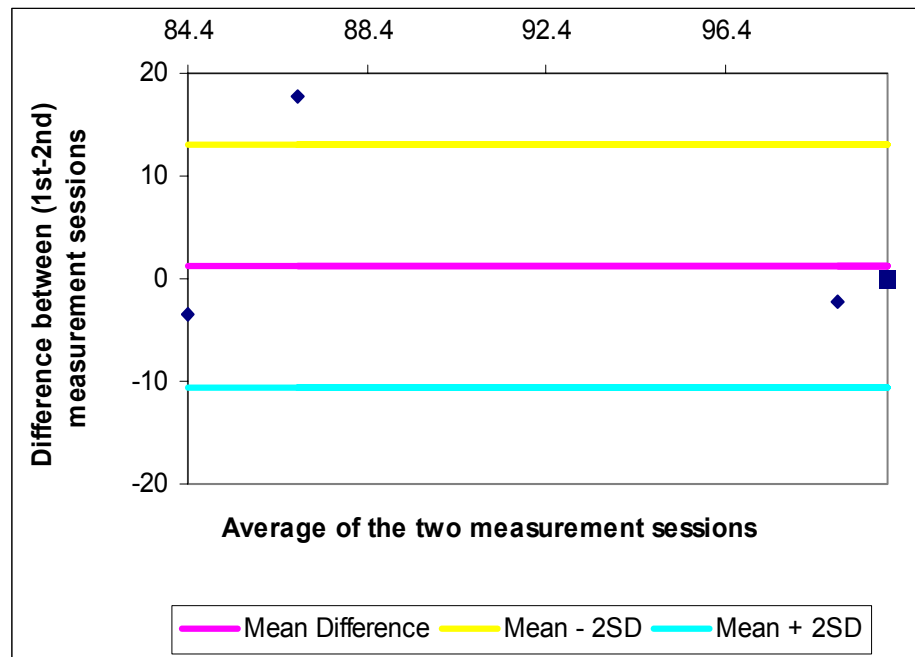
\*Values in median (IQR): IQR = Interquartile range; ICC = Intraclass correlation coefficient.

**Table 6.3: Results of between-days repeatability in children with HMS (n = 10)**  
**Mean (SD) or Median (IQR)**

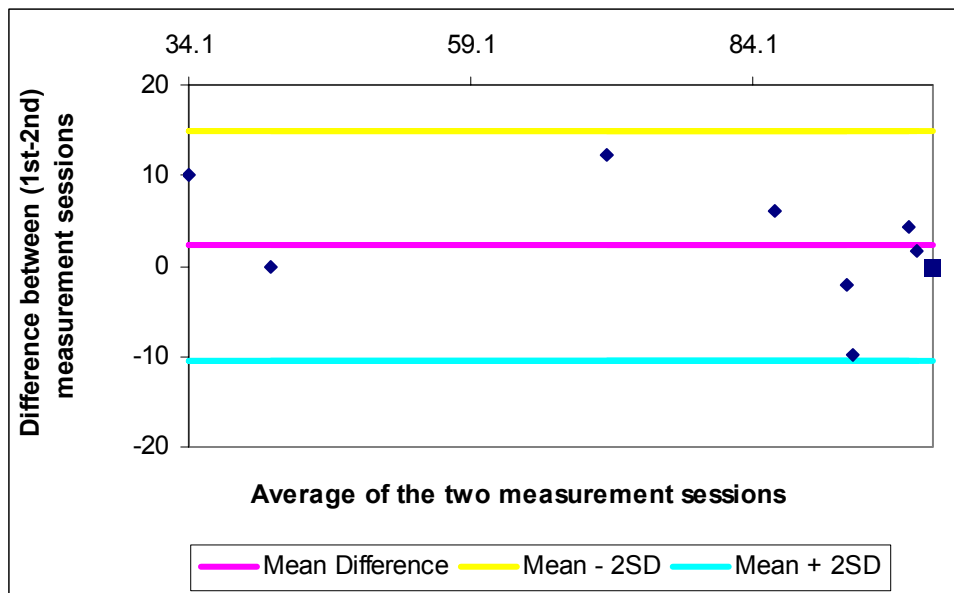
Variable	Day 1	Day 2	ICC	Mean Difference	95% Limits of Agreement
Pain	2.75 (2.91)	2.93 (2.63)	0.80	-0.18	-3.80 to 3.45
*QoL	90.00 (31.8)	85.8 (24.5)	0.87	2.2	-10.4 to 14.9
ROM Extension ( $^{\circ}$ )	-12.20 (1.48)	-12.40 (1.35)	0.90	-0.2	-1.47 to 1.07
ROM Flexion ( $^{\circ}$ )	155.50 (2.80)	155.30 (2.75)	0.96	0.2	-1.38 to 1.78
Muscle Torque Extensors (Nm/kg)	1.30 (0.33)	1.27 (0.27)	0.85	0.03	-0.30 to 0.37
Muscle Torque Flexors (Nm/kg)	0.67 (0.17)	0.67 (0.14)	0.97	0.01	-0.07 to 0.08
Kinaesthesia ( $^{\circ}$ )	3.00 (2.16)	2.70 (1.57)	0.84	0.3	-1.82 to 2.42
JPS at 25 ( $^{\circ}$ )	6.90 (6.54)	6.60 (3.92)	0.56	0.3	-10.76 to 10.16
JPS at 10 ( $^{\circ}$ )	4.90 (3.67)	3.00 (2.63)	0.18	1.9	-5.96 to 9.76
Peak Knee Extension in Mid Stance ( $^{\circ}$ )	-0.73 (3.93)	-1.54 (4.19)	0.68	0.82	-5.74 to 7.38
Knee Flexion During Loading Response ( $^{\circ}$ )	12.86 (4.77)	12.63 (3.38)	0.48	0.22	-8.50 to 8.95
Maximum Knee Flexion ( $^{\circ}$ )	52.98 (3.55)	52.58 (3.41)	0.81	0.39	-4.07 to 4.86

Values are mean (SD), \*values in median (IQR): IQR = Interquartile range; ICC = Intraclass correlation coefficient.

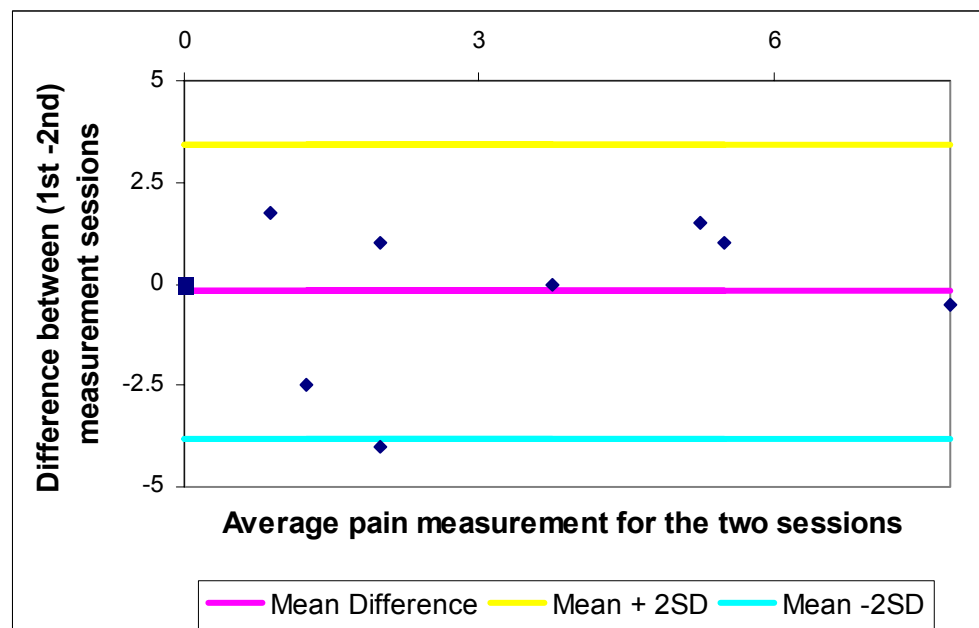
From Figures 6.7 to 6.29 it can be seen that all repeated measurements were within the 95% confidence interval of the mean difference with the exception of QoL measures (Figure 6.7), both extensor and flexor muscle torque (Figures 6.16 and 6.17), and maximum knee flexion during swing phase (Figure 6.29) in the two groups. An outlier each can also be seen for pain measurement (Figure 6.9) in the HMS cohort and all the proprioception outcomes in the HMS group (Figures 6.11, 6.13 and 6.15).



**Figure 6.7: Bland and Altman plots for QoL measurements in healthy children (n = 10). The symbol ■ indicates that seven participants had the same QoL score.**



**Figure 6.8: Bland and Altman plots for QoL measurements in children with HMS (n = 10) – The symbol ■ indicates that two participants had the same QoL score.**



**Figure 6.9: Bland and Altman plot for pain measurements in children with HMS (n = 10) – The symbol ■ indicates that two participants the same zero pain rating.**

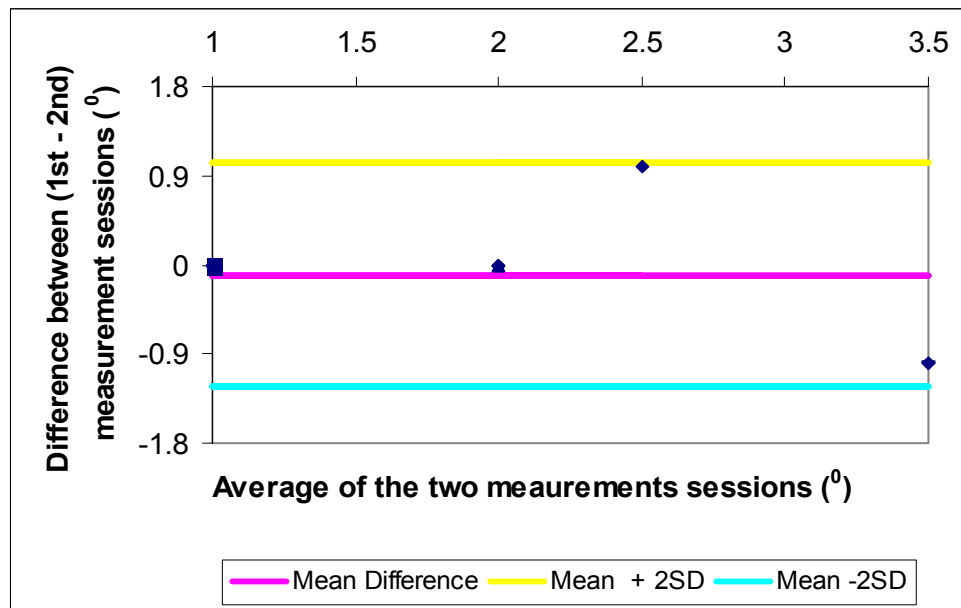


Figure 6.10: Bland and Altman plots for knee joint kinaesthesia showing values of the repeated measurements in healthy children (n = 10) – The symbol ■ and ↑ indicate that three and four participants had the same JK values, respectively.

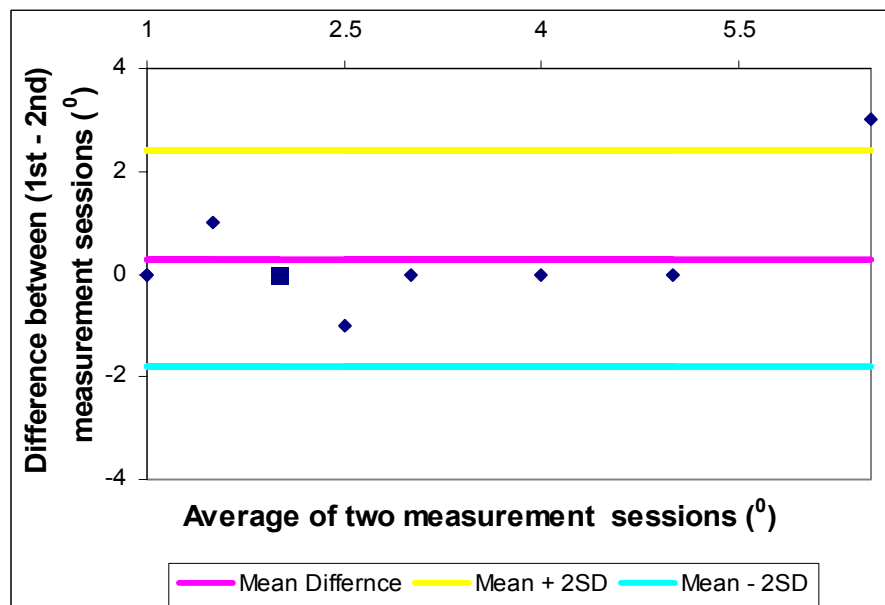


Figure 6.11: Bland and Altman plots for knee joint kinaesthesia showing values of the repeated measurements in children with HMS (n = 10). The symbol ■ indicates that three participants had the same JK value.



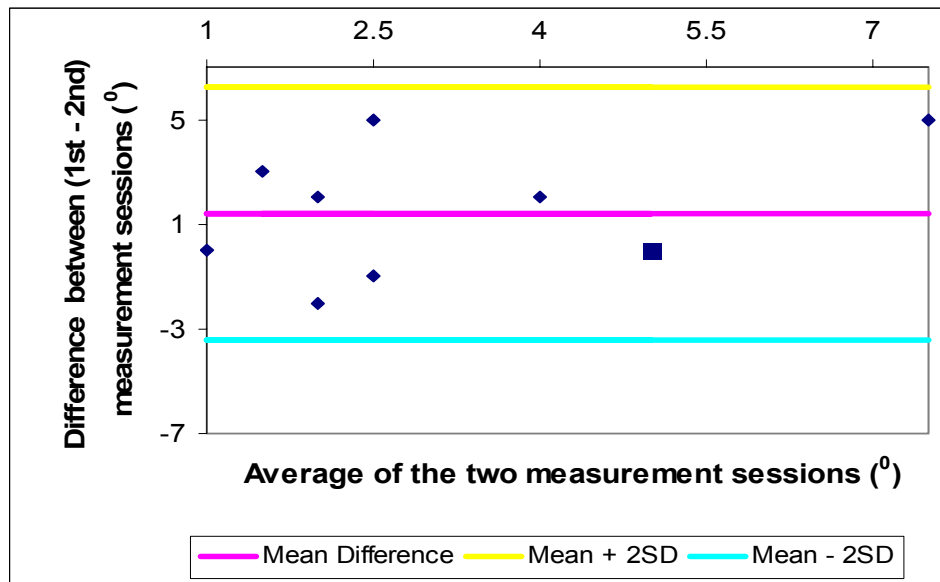


Figure 6.12: Bland and Altman plots for knee JPS at 25° showing values of the repeated measurements in healthy children (n = 10). The symbol ■ indicates that two participants had the same AAE.

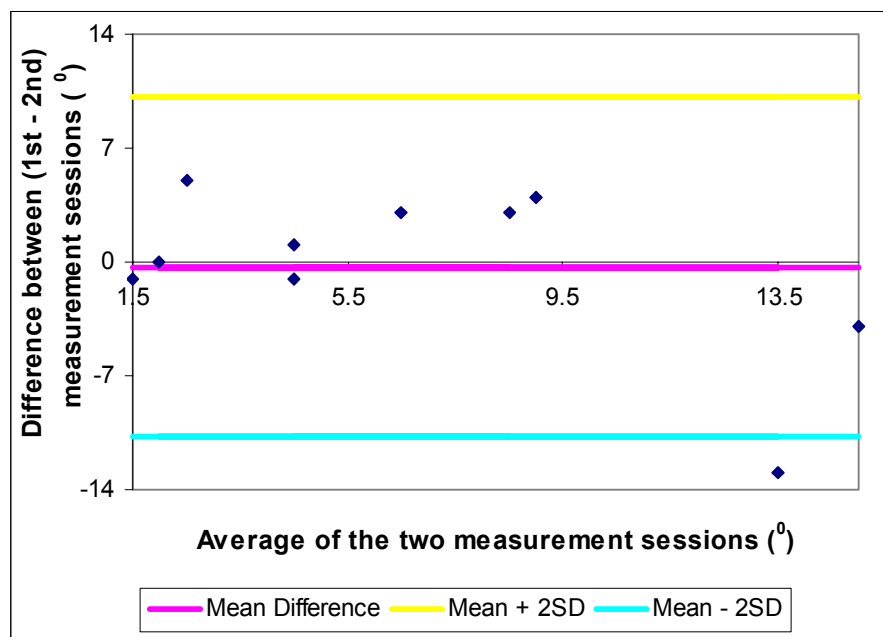


Figure 6.13: Bland and Altman plots for knee JPS at 25° showing values of the repeated measurements in children with HMS (n = 10).

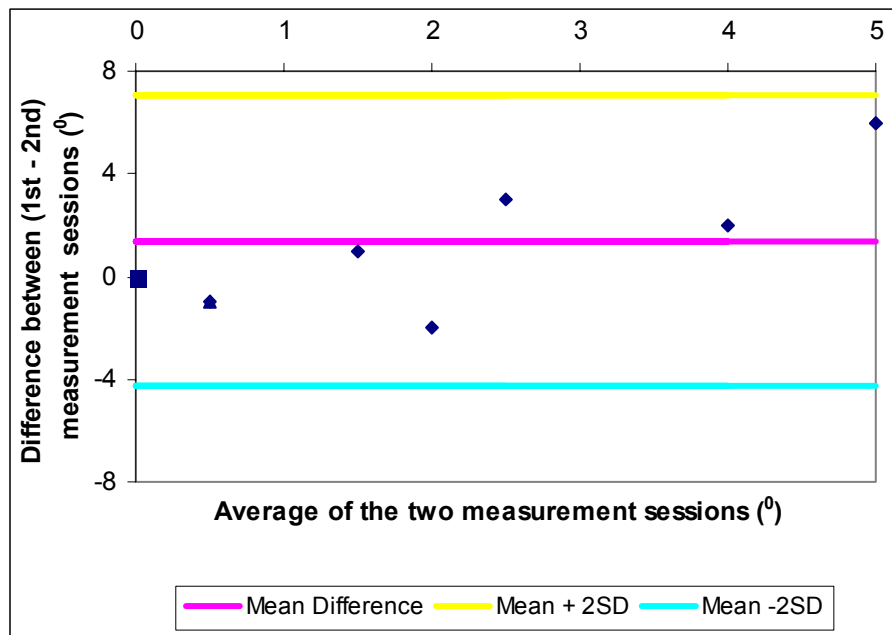


Figure 6.14: Bland and Altman plots for knee JPS at  $10^0$  showing AAE values of the repeated measurements in healthy children. - ■ and ↑ indicate that three and two participants had the same values of AAE respectively.

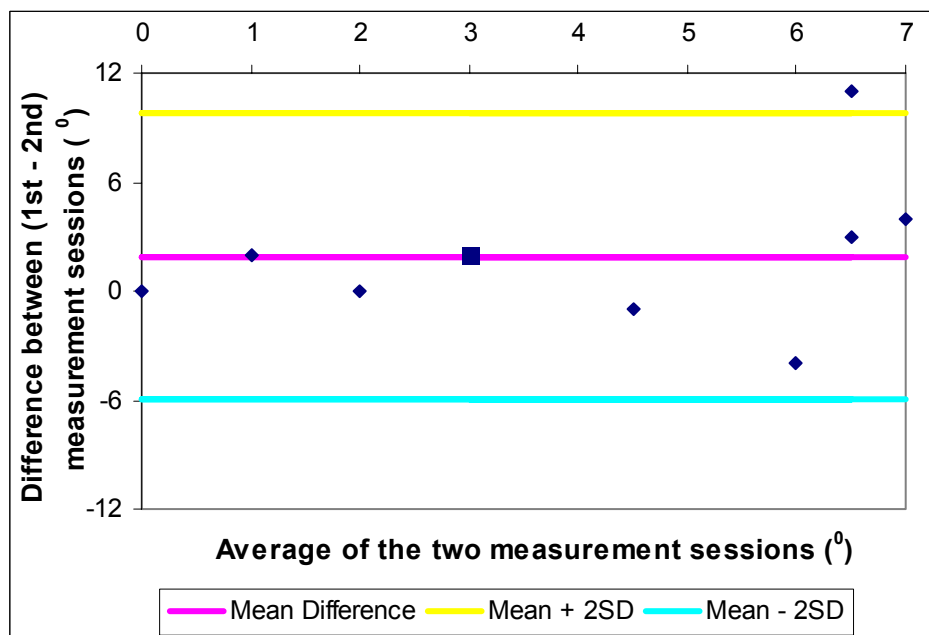
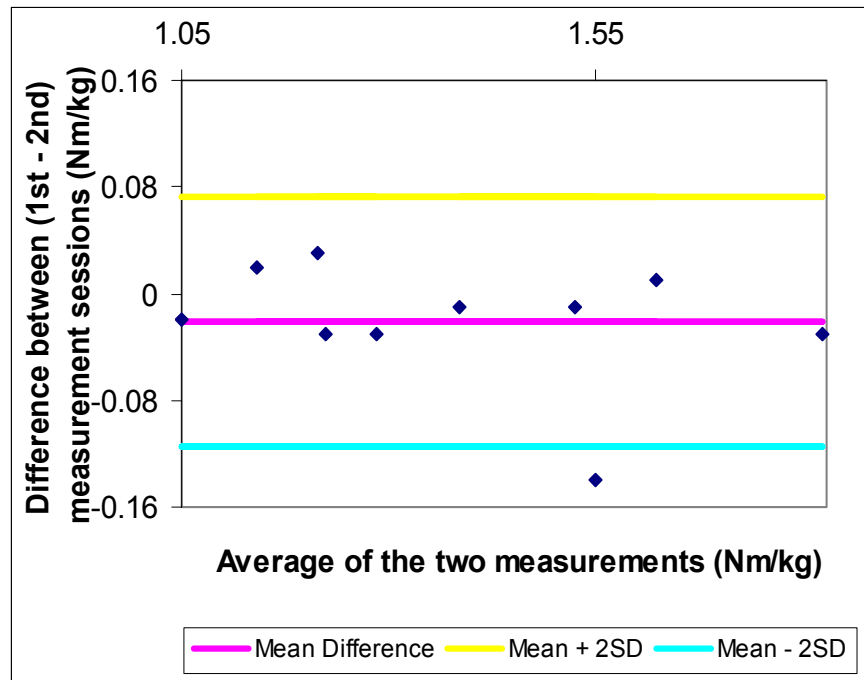
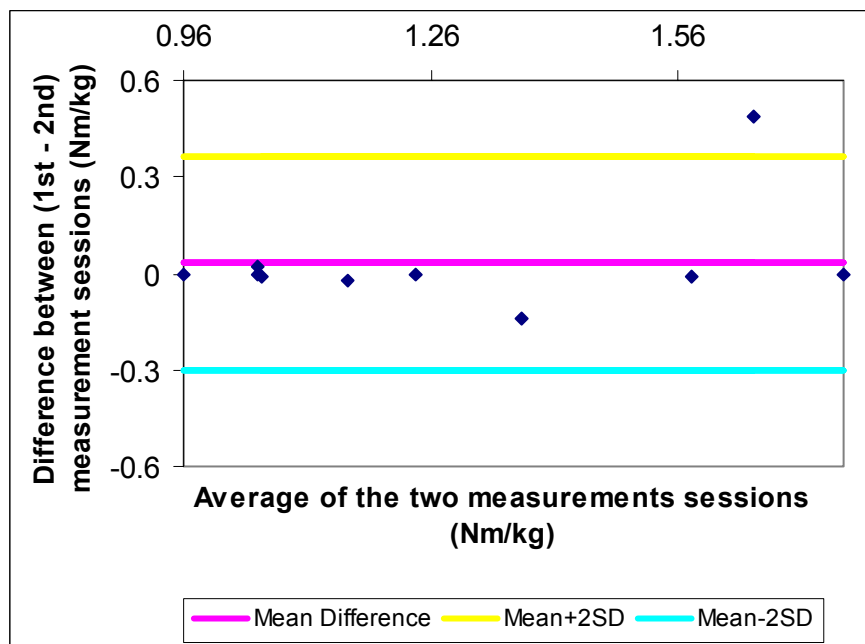


Figure 6.15: Bland and Altman plots for knee JPS at  $10^0$  showing AAE values of the repeated measurements in children with HMS (n = 10). The symbol ■ indicates that two participants had the same values of AAE.



**Figure 6.16: Bland and Altman plot for knee extensor muscle torque showing values of the repeated measurements in healthy children (n = 10)**



**Figure 6.17: Bland and Altman plot for knee extensor muscle torque showing values of the repeated measurements in children with HMS (n = 10).**

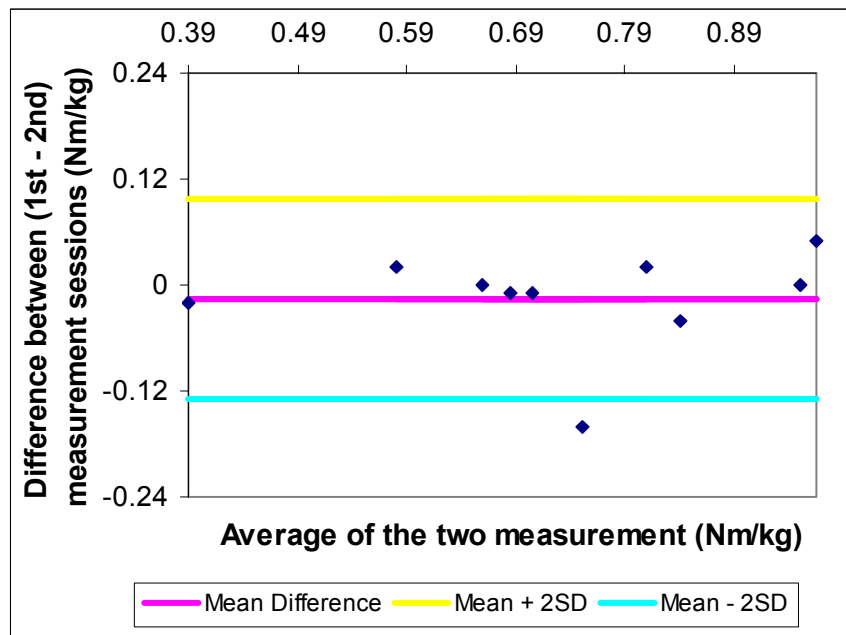


Figure 6.18: Bland and Altman plots of agreement showing the repeated measurements of knee flexor torque in healthy children (n = 10).

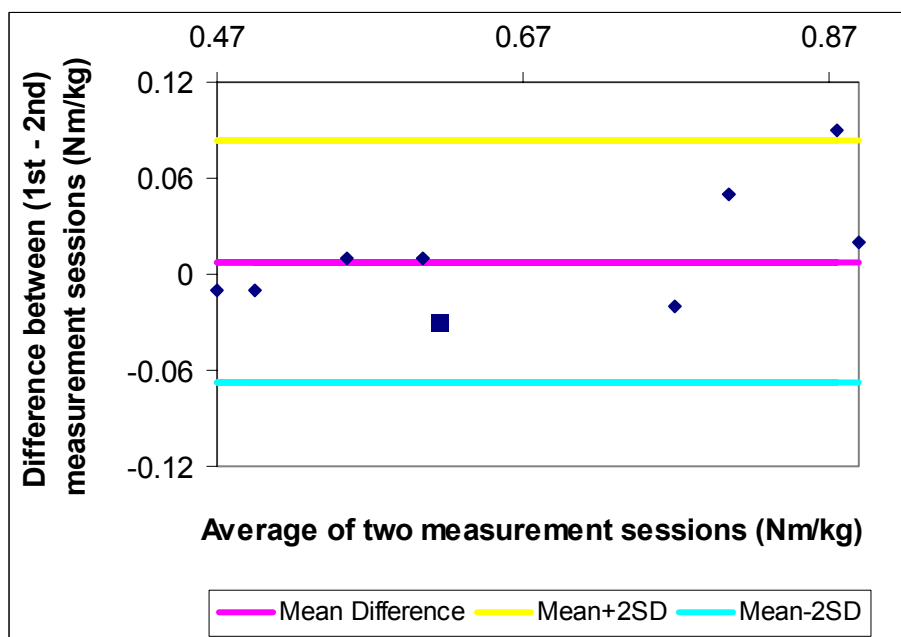


Figure 6.19: Bland and Altman plots of agreement showing the repeated measurements of knee flexor torque children with HMS (n = 10). The symbol ■ indicates that two participants had the same value of extensor muscle torque.

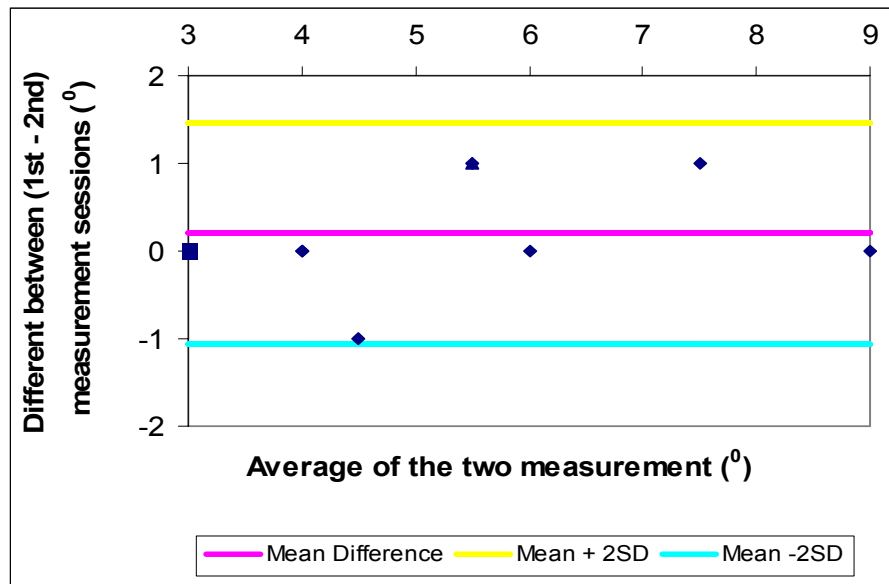


Figure 6.20: Bland and Altman plots for passive knee extension ROM showing values of the repeated measurements in healthy children (n = 10) - ■ indicates three and ▲ shows two participants with same value, respectively.

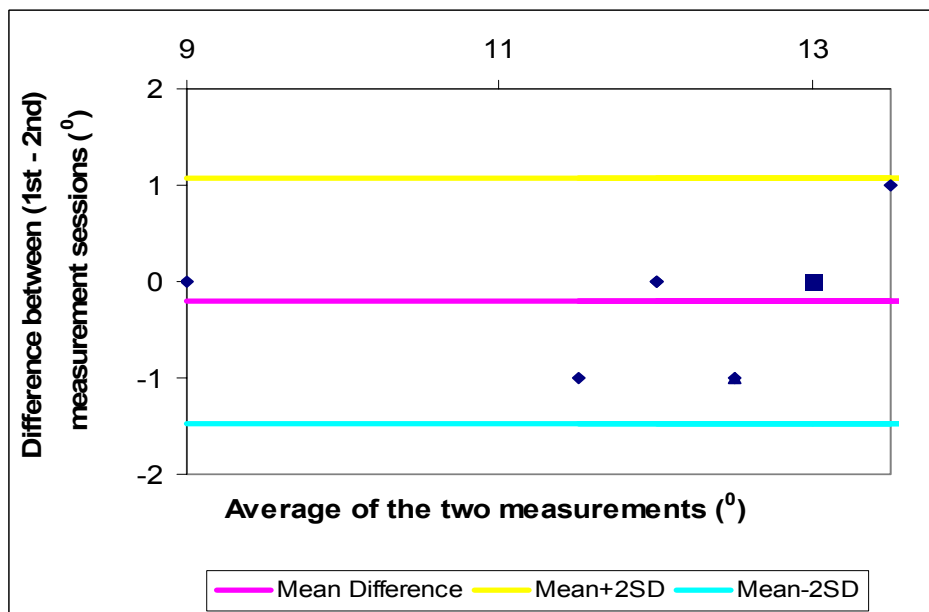


Figure 6.21: Bland and Altman plots for passive knee extension ROM showing values of the repeated measurements in children with HMS (n = 10). Both ■ and ▲ indicate that three participants each had the same ROM values.

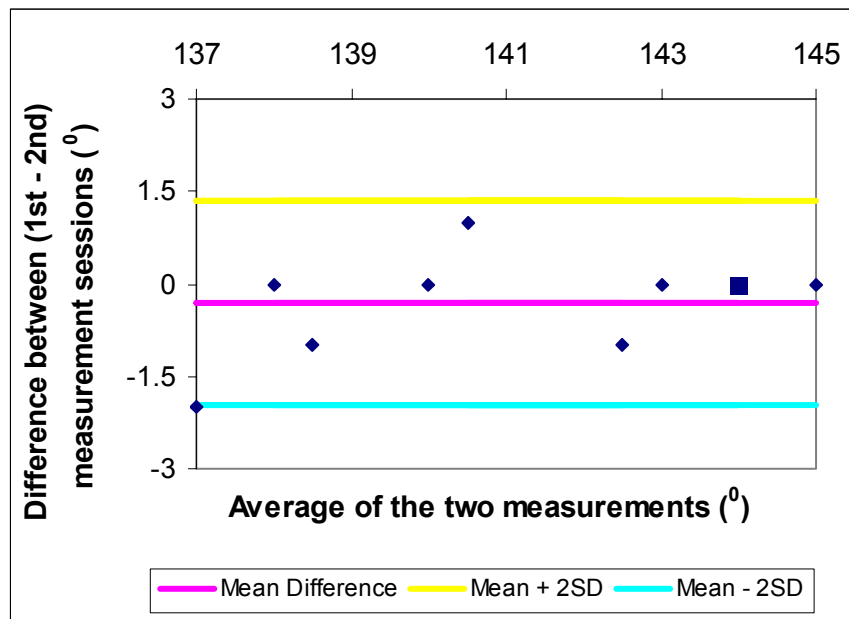


Figure 6.22: Bland and Altman plots for passive knee flexion showing values of the repeated measurements in healthy children ( $n = 10$ ). The symbol ■ indicates that two participants had the same ROM values.

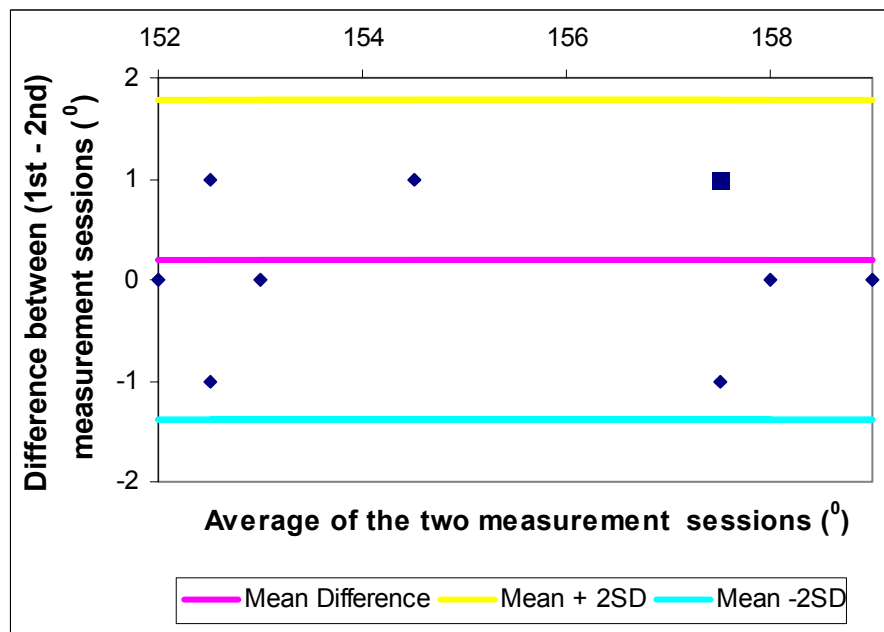


Figure 6.23: Bland and Altman plots for passive knee flexion showing values of the repeated measurements in children with HMS ( $n = 10$ ). The symbol ■ indicates that two participants had the same ROM values.

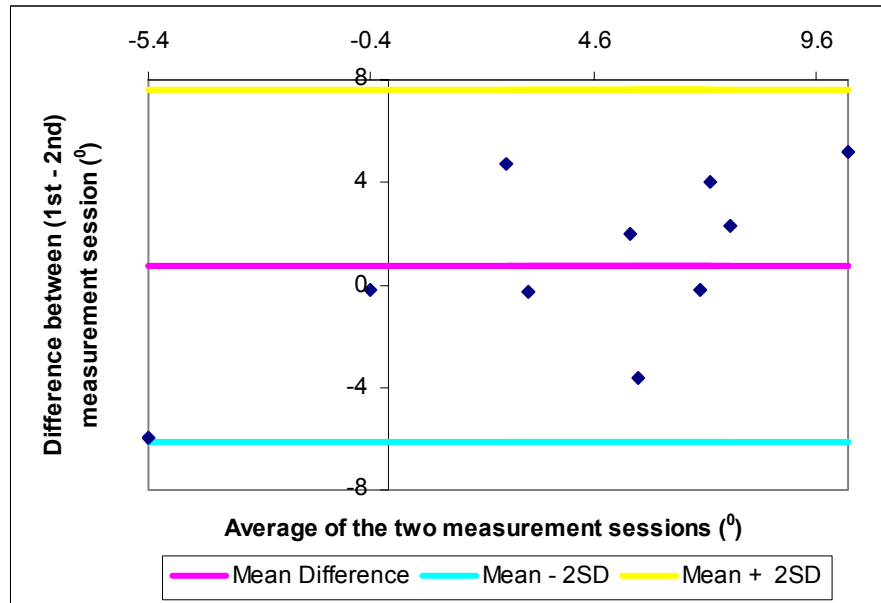


Figure 6.24: Bland and Altman plots for knee extension in mid-stance in healthy children (n = 10).

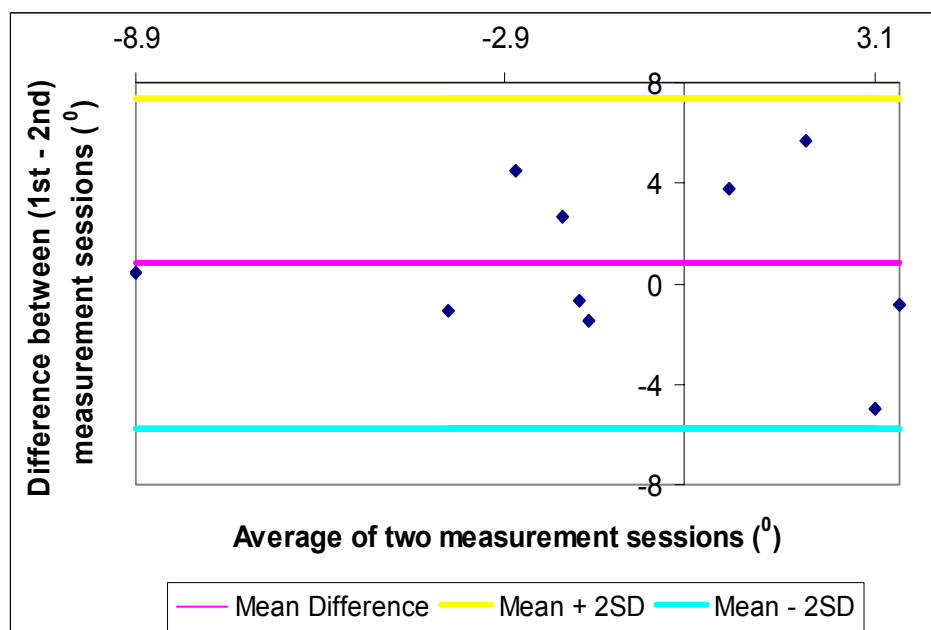
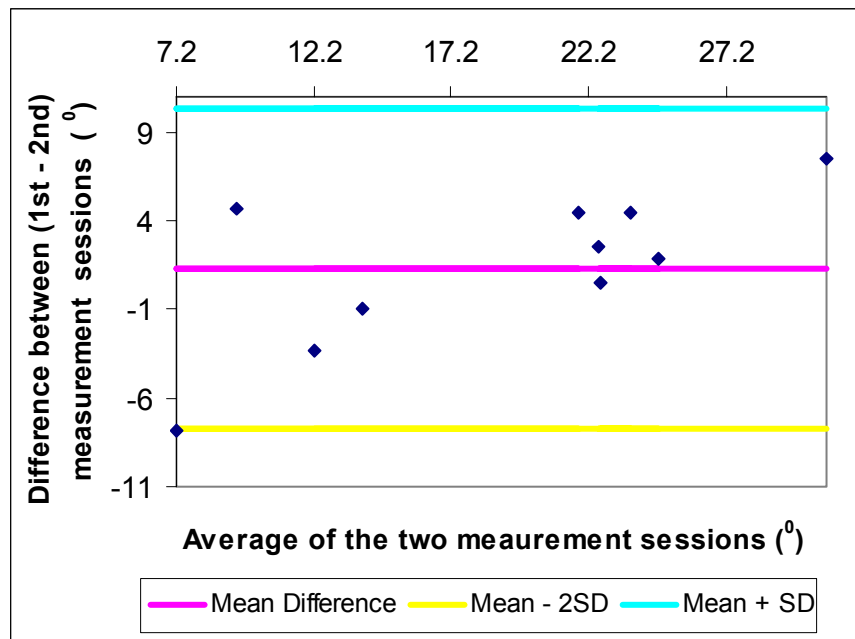
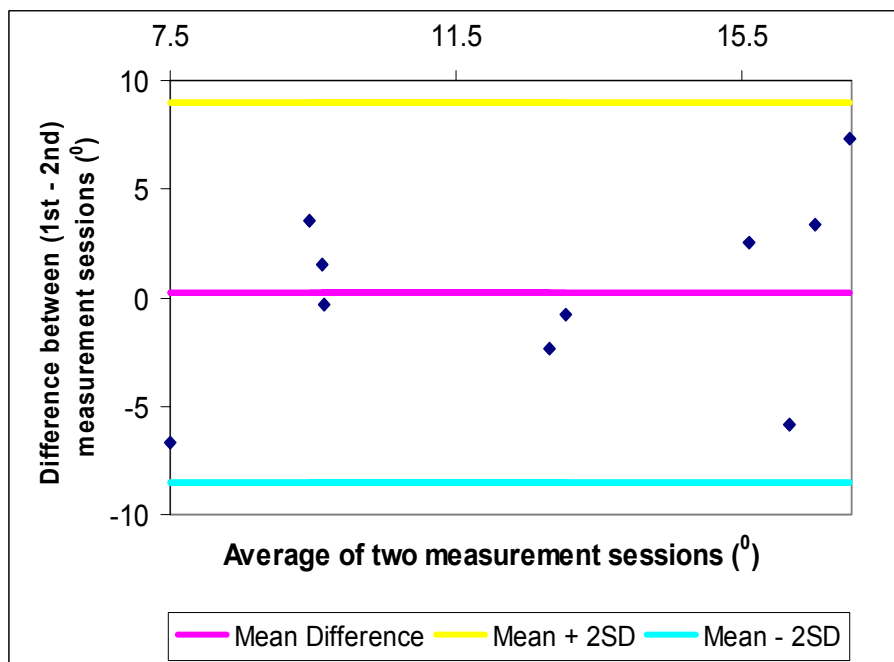


Figure 6.25: Bland and Altman plots for knee extension in mid-stance in children with HMS (n = 10).



**Figure 6.26: Bland and Altman plots for knee flexion during loading response in healthy children (n = 10).**



**Figure 6.27: Bland and Altman plots for knee flexion during loading response in children with HMS (n = 10).**



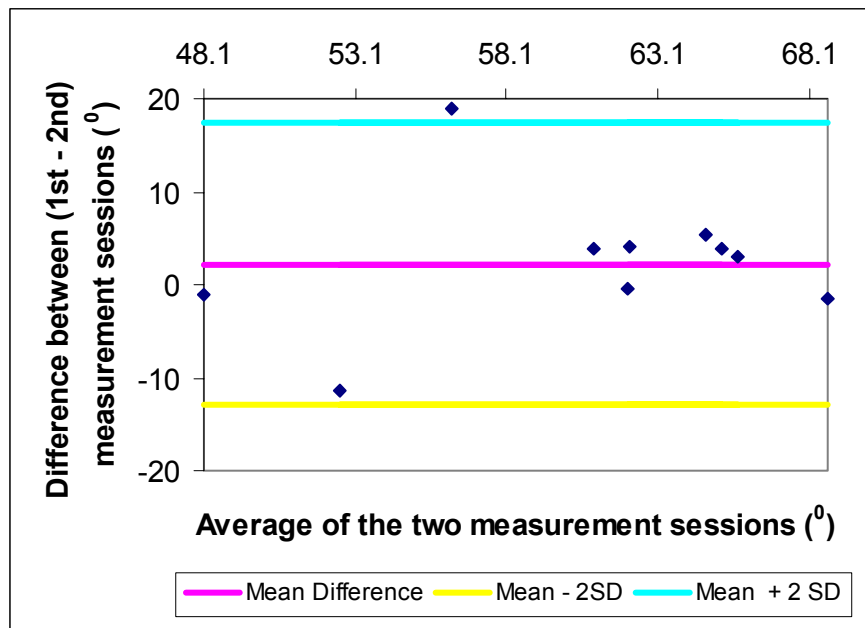


Figure 6.28: Bland and Altman plot for maximum knee flexion during swing phase of walking in healthy children (n = 10).

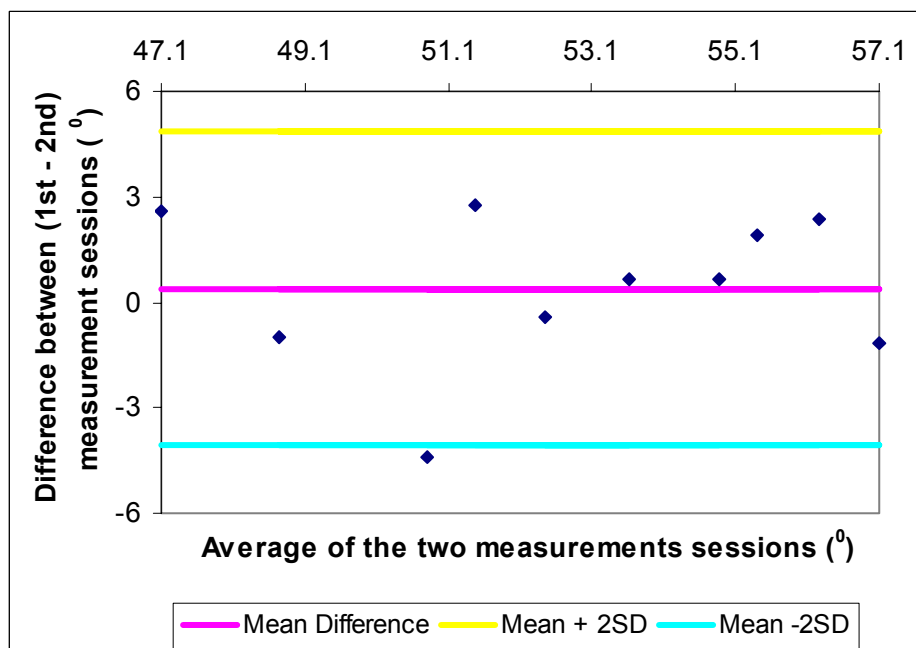
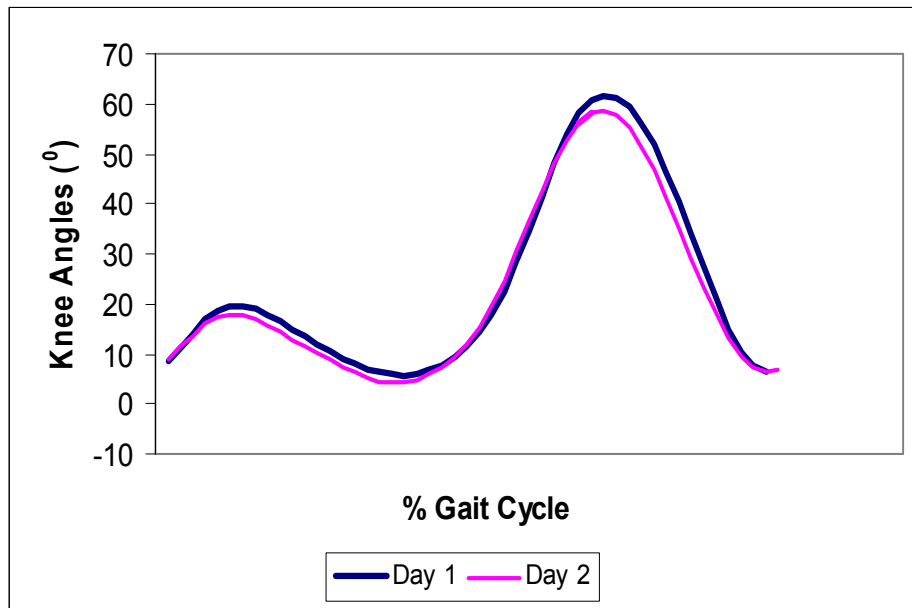
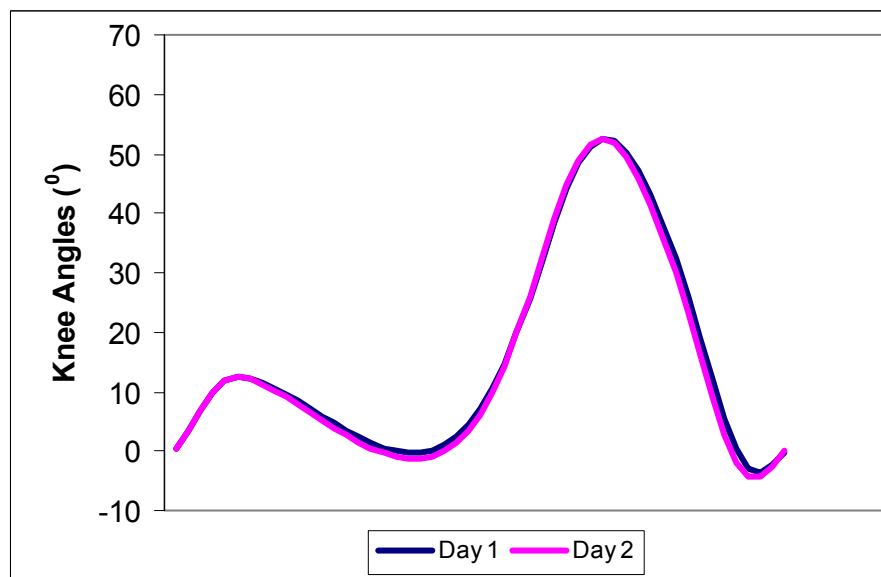


Figure 6.29: Bland and Altman plot for maximum knee flexion during swing phase of walking in children with HMS (n = 10).



**Figure 6.30: Repeated measurements of sagittal knee motion during walking in healthy children (n = 10).**



**Figure 6.31: Repeated measurements of sagittal knee motion during walking in children with HMS (n = 10).**

The highest ICC value was recorded for extension muscle torque in the healthy group while the flexors muscle torque measurements had the highest ICC value in the HMS cohort. JPS at 10° showed the lowest ICC values in both group. 95% LOA indicated that maximum knee flexion measurement had the widest between-days variation and least between-days variation was observed in extensors muscle torque measurement in healthy children. The 95% LOA demonstrated that JPS at 10° had the highest between-days measurement error while flexors muscle torque recorded the least amount of between-days variation in children with HMS. Paired t-test showed no significant difference ( $p$  range = 0.100 to 0.860) between the repeated measurements of JPS in both groups.

Appendix 4.7 (a peer-reviewed article accepted for publication) presents the summary of the findings of repeatability assessment of joint proprioception and muscle torque in healthy children and those with HMS. In addition, the summary of the results of repeatability assessment in both groups presented as a conference paper is illustrated in Appendix 4.3.

#### **6.4.2 Results of the Combined Group of Healthy Children and those with HMS using ICC**

The previous section demonstrated poor to good test-retest repeatability for the JPS tests and some of the sagittal knee motion variables in healthy children (see Table 6.2) and those with HMS (see Table 6.3). These outcomes did not reach the acceptable ICC value of 0.80 (Merlini et al. 1992; Tiffreau et al. 2007) in either healthy children or children with HMS. One of the major limitations associated with the use of ICC is that its magnitude is highly dependent upon sample heterogeneity (Batterham and George 2000), that is the between subject variation. The greater the range or spread of measurements obtained, the greater the magnitude of ICC. The low ICC values obtained for the outcomes (Tables 6.2 and 6.3) may be due to the homogeneity of the respective samples (healthy, HMS) used as this could create between subjects variance. Therefore, it is possible that ICC values for the heterogeneous group (i.e combination of healthy children and those with HMS) will be different from those obtained for a two independent homogeneous samples. The two sets of data for proprioception and knee kinematics in healthy children and those with HMS were therefore combined and further analysed for test-retest repeatability using ICC. Similarly, functional ROM data in both groups were

combined and further analysis was performed using ICC. The mean (SD) and ICC values of all measurements (day 1 and 2) are presented in Table 6.4.

**Table 6.4: Results of between-days repeatability in healthy children and children with HMS (n = 20): Mean (SD) and ICC values.**

Variable	Day 1	Day 2	ICC
JPS at 25 ( $^{\circ}$ )	5.30 (3.53)	4.75 (5.20)	0.58
JPS at 10 ( $^{\circ}$ )	3.85 (3.54)	2.20 (2.12)	0.26
Peak Knee Extension in Mid Stance ( $^{\circ}$ )	1.99 (5.63)	1.19 (4.72)	0.79
Knee Flexion During Loading Response ( $^{\circ}$ )	16.23 (8.06)	15.42 (5.70)	0.81
Maximum Knee Flexion ( $^{\circ}$ )	57.43 (7.55)	56.00 (6.37)	0.68

SD = Standard deviation; ICC = Intraclass correlation coefficient.

The ICC value for knee flexion during loading response was high (0.81) indicating excellent agreement between repeated measurements. However, the two JPS tests, knee extension in mid stance and the maximum knee flexion in swing phase during level walking had low ICC values (range = 0.26 – 0.79) suggesting poor to good agreement between repeated measurements by the researcher. Analysis of the combined data from the two different homogeneous samples of healthy children and those with HMS yielded a higher value of ICC for JPS at 25 $^{\circ}$  than either of the two independent groups. In addition, ICC value for JPS at 10 $^{\circ}$  in the combined group was higher than in the HMS group. These values did not reach the acceptable value of 0.80 however. For functional ROM, the ICC value of knee extension was higher in the combined group than either the healthy or HMS cohorts. Maximum knee flexion had a higher ICC value than the healthy group, but lower than the HMS cohort. This value was also below the acceptable value of 0.80.

Based on the findings of the analysis of the combined data, it seems that the poor to good test-retest repeatability for the JPS tests and some of the sagittal knee motion variables in healthy children and those with HMS (see Tables 6.2 and 6.3) might not have been due to the homogeneity of the samples.

## 6.5 Discussion

The test-retest repeatability of each component of the assessment method was examined in 20 children (10 healthy and 10 children with HMS). Each participant was assessed for test-retest repeatability on two different occasions (one week apart). Data analyses were carried out using 95% limits of agreement (LOA) and Intraclass Correlation Coefficient (ICC) (Rankin and Stokes 1998; Potter et al. 2006). The results of the test-retest repeatability of the outcome measures and possible sources of variation are acknowledged in this section.

Overall, the findings of the test-retest repeatability in children diagnosed with HMS were similar to those reported in healthy children with 8 of the 12 variables having ICC values ranging from 0.80 – 0.98. However, the ICC values for both JPS (at 25° and 10°) were low in both groups (range = 0.18 to 0.56). Similarly, low ICC values were recorded for the knee kinematic tests in healthy children (knee extension in mid stance, ICC = 0.74; maximum knee flexion, ICC = 0.48) and those with HMS (knee extension in mid stance, ICC = 0.68; knee flexion during loading response, ICC = 0.48). The sets of data for both JPS and knee kinematic tests in healthy children and those with HMS were combined for further analysis using ICC. The ICC values for the combined group were still below the acceptable value for the JPS tests, knee extension in mid stance and during maximum knee flexion (ranged from 0.26 – 0.79).

No previous studies were found investigating the test-retest repeatability of any of the knee joint proprioception outcomes in children. There is also limited information on the test-retest repeatability of pain, knee muscle torque, knee kinematics and QoL in children. Therefore, the findings of the present study are discussed in relation to previous results of repeatability on these outcomes in adults with HMS (Ferrell et al. 2004) and children with other pathological conditions (McCarthy et al. 2005).

Based on ICC, the repeatability of QoL measure was higher in the healthy cohort than in the HMS group. This may be due to larger between-days variation in the HMS group than healthy children. The findings of the present study on QoL measures in children with HMS are in agreement with the findings reported by McCarthy et al. (2005) and those of Ferrell et al. (2004). McCarthy et al. (2005)

observed a good to excellent test-retest repeatability ( $r$  range = 0.75 - 0.90) of PedsQL in children with traumatic brain injury. Ferrell et al. (2004) also found that global SF – 36 scores did not differ significantly ( $p = 0.90$ ) between two repeated measurements (2 – 8 weeks apart) in 10 adults with HMS indicating that there was a good agreement between the measurements. The observations in the present study indicate that QoL perception can be measured in healthy children and those with HMS by the researcher with minimal between-days variation.

Repeatability of pain measures with the CAS in the HMS cohort was excellent. The results obtained in the present study confirm the reports of previous investigators who found excellent repeatability of pain assessment using a visual analogue scale (VAS) in healthy children aged 9 -15 years (McGrath et al. 1987). ICC values for knee extension and flexion measurements in the present study were high (range = 0.90 – 0.96) in both groups.

The results of the present study on knee PROM are in agreement with the findings of Pandya et al. (1985) who reported an excellent test-retest repeatability (ICC range = 0.81 to 0.91) of passive knee extension measurements in patients with Duchenne muscle dystrophy aged 1 - 20 years, using a universal goniometer. The ICC value (0.90) of extension ROM in children with HMS was slightly lower than in healthy children (0.95). However, ICC values (both 0.96) were similar for flexion ROM in both groups. The 95% limits of agreement for both extension and flexion ROM measurement were low (Tables 6.2 and 6.3). The findings of the present study indicate excellent repeatability of passive knee ROM measurements. The results of the current investigation suggest that PROM of the knee joint in healthy children and children with HMS can be assessed by the researcher using a universal goniometer with a small amount of between-days variation.

Test-retest repeatability of muscle torque has been investigated in children using a hand-held myometer (Effgen and Brown 1992) and digital myometers (Seniorou et al. 2002; van der Linden et al. 2004). Effgen and Brown (1992) examined the test-retest repeatability of a hand-held myometer in 12 children with myelomeningocele aged 9.8 - 17.4 years. Both upper and lower limbs muscles were tested twice (23 days interval) in their study. They found ICC values for the upper limb muscles to be 0.75 – 0.99 while those of the lower limb were 0.73 – 0.94. The ICC values for knee

flexors and extensors muscle torque were reported to be 0.73 - 0.86 (range). In the current study, ICC values for healthy children and those with HMS ranged from 0.85 to 0.98. These values are higher than those obtained in Effgen and Brown's study. A hand held-myometer was used in Effgen and Brown's study while a fixed myometer was used in the present study. A potential limitation of hand-held myometers is that subjects' limbs are difficult to stabilise during testing. This could have affected the measurement protocol used by Effgen and Brown (1992) as this was not standardised in their study. In the current investigation, subjects were retested one week apart while participants were tested 23 days apart in that study. Since the level of physical activity participation of participants in the present study was not taken into consideration as such in the study of Effgen and Brown (1992) therefore it is difficult to say whether this had an effect on their results.

Furthermore, the results of knee extensors and flexors muscle torque obtained in this study confirm the findings of Seniorou et al. (2002) who recorded an excellent test-retest repeatability of knee extensors (ICC = 0.95) and flexors (ICC = 0.93) muscle torque in healthy children aged 5 – 16 years, using a fixed myometer. The ICC value (0.85) recorded in children with HMS for knee extensors in the present study is similar to that (ICC = 0.84) reported in children with cerebral palsy (CP) by Seniorou et al. (2002). However, a higher ICC value of 0.97 was obtained for knee flexors in children with HMS in the current study while the ICC value reported by Seniorou et al. (2002) for knee flexors in children with CP was 0.70. The observed difference in repeatability of knee flexors may be due to the differences in participants' characteristics. The findings of the current study showed that knee extensors and flexors muscle torque can be measured by the researcher with excellent repeatability in healthy children and those with HMS, using a fixed digital myometer.

The findings of repeatability of JK were excellent in both healthy children and children with HMS (ICC range = 0.83 - 0.84). However, poor repeatability was recorded for both JPS tests in both groups (ICC range = 0.18 – 0.26). The present study indicates that JK test was more repeatable than JPS tests. Thibault et al. (1994) examined the between-days (14 days apart) repeatability of wrist, shoulder, hip and ankle JK in 43 healthy children aged 6 – 12 years. They reported an excellent Kappa coefficient of 0.81 (mean) (range 0.37 – 1.00) for all measurements.

It is difficult to compare the results of these authors with the findings of the present study for two reasons. First Thibault et al. (1994) examined the joints of both upper and lower limbs (excluding the knee joint) while the knee joint was tested in the current study. Secondly, Kappa coefficient was used for test-retest repeatability analysis in their study while ICC and 95% LOA were used in the present study. The use of Kappa coefficient test-retest repeatability analysis by Thibault et al. might not have been appropriate, as it is used to examine inter-observer repeatability for two nominal variables (Morgan et al. 2004; Sim and Wright 2005). The results observed on JK in the current study are in agreement with the studies of Beynnon et al. (2000) and Cross et al. (2005). They found knee JK to be more repeatable than knee JPS. Yan et al. (2000) also demonstrated excellent repeatability of knee JK in healthy elderly (ICC = 0.90 – 0.98) and healthy young (ICC = 0.85 – 0.98) adults.

On the other hand, the findings of the present study contrast with the results of Barrett (1991) who reported a Pearson correlation coefficient of 0.82 when repeatability of knee JPS was evaluated in 20 healthy adults. Pearson correlation is a measure of linear association (relationship between two measurements) (Bland and Altman 1986) and not repeatability (the extent to which measurements agree) (Bland and Altman 1996a; Batterham and George 2000). Pearson's correlation coefficient tends to increase when the spread of the data is large (Bland and Altman 1996a; Batterham and George 2000). In Barrett's study, subjects' limbs were moved passively by the investigator, whereas a purpose-built motorised device was used in the present study. Subjects were tested in a sitting position in the present experiment while they examined their participants in a supine position. In supine participants are more relaxed than in sitting therefore this factor might have contributed to the ability of participants to accurately detect their JPS in a more repeated manner as observed by Barrett (1991). In addition, Barrett did not state the interval between the two sets of readings used to calculate the repeatability. It is possible that both readings were carried out within a day as the closer the testing sessions the lower the measurement errors (variations) that are likely to be recorded (Domholdt 2000). These methodological differences could have accounted for the contrasting results obtained.



Low repeatability of JPS tests (ICC = 0.18-0.58) obtained in the present study also contrasts with the results of Tsang and Hui-Chan (2003). They found between-days (1 week apart) repeatability of passive JPS to be excellent (ICC = 0.90) in eleven healthy elderly subjects (mean age  $\pm$  SD = 70.8  $\pm$  4.0 yrs). There are a few potential reasons for this discrepancy. In the study by Tsang and Hui-Chan (2003), subjects were tested in sitting with the knee at a starting angle of 30° and test angle of 3° flexion. Whereas, in the present study the starting knee angle was 90° and the test angles were 25° and 10° flexion. It has been reported that joint mechanoreceptors are more sensitive near end range of knee extension (Lephart et al. 1992; Borsa et al. 1997). Since the test angle of the knee joint used in Tsang and Hui-Chan's study was closer to the end range of knee extension than in the present investigation, it is possible that the knee joint mechanoreceptors in their subjects were somewhat more activated. Therefore, the present results on JPS could have been due to the test angles of the knee joint. The low repeatability of JPS measurements in the present study could be due to the participants' age. It has been found that proprioceptive acuity decreases with increase in age in adults (Skinner et al. 1984; Hurley et al. 1998) but increases with advancing age in children (Visser and Geuze 2001; Goble et al. 2005). Growth spurts in children are believed to be accompanied by stretching of the collagen (Bird 2005) and this may therefore cause a temporary proprioception deficit in children compared with adults.

Cutaneous input was minimised by means of an air splint in the study by Tsang and Hui-Chan (2003). However, cutaneous input was not minimised in the present study using an air splint. It is believed that air splints, in addition to minimising cutaneous sensation may stimulate articular pressure-sensitive mechanoreceptors (Stillman 2000). Again, the findings of Tsang and Hui-Chan, (2003) could be the result of the air splint used as this could also have enhanced the proprioceptive acuity of their participants and may have resulted in the better test-retest repeatability reported in their study.

The mean AAE for both JPS at 25° and 10° decreased during the second session in both healthy children (Tables 6.2) and those with HMS (Table 6.3), suggesting that learning effects previously observed in healthy children (section 5.7.7) might have been a factor. These decreases were not statistically significant (paired t-test p range = 0.100 to 0.860), however. Testing was carried out at different times during

the two sessions, which might have led to the results obtained. Some participants came directly to the lab after school during the first visit and they attended the lab directly from home during the second visit, as the following week coincided with school holidays. This could have led to fatigue on the part of the participants coming directly to the lab from school.

Cognitive distraction during testing has been reported to affect JPS testing (Taylor et al. 1998). The presence of other people in the lab during testing might have affected the children's level of concentration. In addition, the limb support used for testing was found to be small for some participants, and could have resulted in difficulty for the researcher to align subjects' knee joint flexion-extension axis with the centre of rotation of the driving shaft. This might have led to error in the ability of the researcher to identify and align the knee axis in a repeated manner. This is an important consideration as test-retest/intra-rater repeatability of identifying the knee flexion-extension axis was not examined in this thesis but could be an area for future research.

Based on the results of ICC, knee flexion during the loading response and maximum knee flexion were observed with excellent repeatability in healthy children (ICC = 0.84) and those with HMS (ICC = 0.81) respectively. However, 95% LOA showed small between-days measurement error for functional ROM in healthy children, with the exception of maximum knee flexion. In addition, LOA demonstrates minimal variation during repeated measurements of knee kinematics in children with HMS, indicating excellent repeatability with the exception of maximum knee flexion in healthy children. These findings are in agreement with those of Gorton et al. (1997). They reported low between-days repeatability of knee joint kinematics in healthy children using the VICON system.

Marker placement was carried out by the investigator on successive days of testing in the current study. Despite the extreme care taken in the marker placement procedure, it was difficult to align the knee joint axis of rotation repeatedly. Therefore, the results of knee joint kinematics may also be due to errors in determining the knee joint centre correctly (Leardini et al. 1999). The markers were susceptible to skin movement that could also have influenced the knee kinematic measures. Finally, each individual's walking pattern may be affected by mood and

fatigue (Beck et al. 1981). All these could have affected the between-days repeatability of knee kinematics in this study.

Since children with HMS may present with pain, it was anticipated that repeatability was going to be poorer in children with this condition than the controls. However, the findings of knee muscle torque assessment were similar in both groups. Another interesting observation in the present study was the between-days variation in knee kinematic measurements which was lower (based on 95% LOA) in the HMS group than in controls. The reasons for these findings are not readily known. It has been reported that muscle torque improved with increasing age in children (Barber-Westin et al. 2006; Eek et al. 2006). Gorton et al. (1997) found that younger children had lower between-days repeatability of knee kinematic measurements than their older counterparts. Therefore, the results obtained in the current study may be due to the age difference of the participants, as the HMS cohort was on average 2 years older than the healthy group.

There are some limitations to this study. First, only the knee joint was tested in the present study thereby limiting the generalisability of the findings to other joints. Secondly, the participants in the present study were healthy children and those with HMS. Therefore, the findings should be extrapolated to other groups with caution. Additionally, the limited number of participants in this study may have contributed to false negative findings (Type 2 errors) in relation to JPS and knee joint angles during walking. The findings do, however, provide important preliminary data on the test-retest and intra-rater repeatability of knee joint proprioception, muscle torque, pain, QoL and passive ROM in children with HMS.

## **6.6 Conclusion**

In conclusion, the neuromuscular, functional ROM and QoL indices measures were repeatable in healthy children and those with HMS. Of the 12 outcome measures assessed 4 (the 2 JPS tests and 2 variables of functional ROM during walking) did not reach the acceptable level of ICC value for repeatability in both groups. These findings suggest that, using these assessments, clinicians could measure pain, JK, muscle torque, passive ROM and QoL repeatedly in children diagnosed with HMS. Such assessments could be used to identify impairments, QoL and changes over time, thereby influencing treatment plans for children with HMS. Furthermore, JPS tests and knee kinematics in children should be used with caution.

The results of this study revealed that between-days repeatability in children diagnosed with HMS was similar to that obtained in healthy children. In general, all the potential sources of variability can be expected to influence the between-days repeatability of both JPS tests and knee kinematic data. The sample size used in the present study was small; therefore, it may be necessary to develop a profile of repeatability characteristics for healthy children and those with HMS using a larger sample size. Moreover, examination of raw data of the subjects (the two JPS and knee kinematics) revealed that there was a small between subjects variability. This could have accounted for the low ICC values obtained for these measurement parameters. The limitation of the ICC is that it is strongly influenced by the magnitude of the variance between subjects (Batterham and George 2000). Therefore, to overcome this limitation, it is recommended that the ICC should be combined with other methods of repeatability analysis such as 95% LOA. The present study was carried out on the knee joint, limiting the generalisability of the results to other joints.

Due to the developmental nature of the present study and time spent on the validation and repeatability experiments, the within-day and inter-rater repeatability of the outcome measures could not be investigated. It is acknowledged that for broader use and applicability, other aspects of repeatability of the outcome measures should be investigated. This is an area for further study.

## **6.7 Overall Summary**

This chapter has reported the test-retest (intra-rater) repeatability of the outcome measures used in the present study. The assessment methods for children diagnosed with HMS demonstrated, in general, excellent test-retest repeatability. The test-retest repeatability for JPS tests and functional ROM measurements using ICC and 95% LOA in healthy children, those with HMS and the combined group were not as high as those for QoL, pain, JK, muscle torque and ROM. However, JPS test and functional ROM were still examined in the present study as the researcher believes that the low repeatability may not limit the ability of their measures to detect any group difference in a cross-sectional study, since the assessment will be carried out on just one occasion (Petrie et al. 2002; Mann 2003; Levin 2006).

From these test-retest (intra-rater) repeatability experiments it was decided that there was sufficient evidence of repeatability to merit further use of the measures to determine the neuromuscular performance, functional ROM and QoL characteristics in larger healthy and HMS cohorts. This testing procedure was therefore used during data collection in both healthy children and those with HMS.

The following chapter present the methods and results of the assessment of healthy children and those with HMS.

## **CHAPTER 7 : ASSESSMENT OF HEALTHY CHILDREN AND THOSE DIAGNOSED WITH HYPERMOBILITY SYNDROME**

### **7.1 Introduction**

Having established an acceptable level of repeatability of the testing procedure, a study was carried out to fulfil the remaining aims of the research. An assessment of healthy children and those diagnosed with HMS (based on the Beighton criteria) was carried out. This chapter outlines the experimental design and the recruitment of healthy and experimental subjects. In addition, the results of neuromuscular performance, functional ROM and quality of life (QoL) characteristics in healthy children, those with HMS and the comparisons of the two groups are presented.

### **7.2 Methods**

#### **7.2.1 Research Design**

A cross-sectional design was used in the present study. However, the test-retest repeatability of the outcome measures and intra-rater repeatability was also investigated to justify the generalisability of the findings. A cross-sectional study is usually conducted to estimate the prevalence of the outcome of interest for a given population, where data can be collected on individual characteristics at only one point in time (Petrie et al. 2002; Mann 2003; Levin 2006). Levin (2006, p. 25) stated that “cross-sectional studies provide a 'snapshot' of the outcome and the characteristics associated with it, at a specific point in time”. A cross-sectional study is a valuable design that can be used in cases where the 'gold standard' of study design (double blind randomised controlled or randomised controlled trials (RCTs)) cannot be used due to ethical reasons (Mann 2003). RCTs may be expensive and may require a large sample size and lengthy periods to generate data.

On the other hand, a cross-sectional study is easy, inexpensive and less time consuming than RCTs (Petrie et al. 2002; Man 2003; Levin 2006). In a cross-sectional design, fewer subjects are needed. The prevalence of the outcome of interest can be estimated because the sample is usually taken from the whole population (Mann 2003; Levin 2006). This design can be used for assessing many outcomes or variables in one study (Mann 2003; Levin 2006). It is also useful for public health planning, understanding disease aetiology and for the generation of hypotheses (Levin 2006). In addition, a cross-sectional study is not associated with the risk of loss to follow-up as participants are examined once (Levin 2006). The

following are possible limitations of a cross-sectional study: it does not provide an explanation for its findings (Mann 2003); observations from a 'snap shot' in a cross-sectional study may not be a true reflection of the studied population as differing results may be obtained if another time-frame had been chosen (Levin 2006); this design cannot be used effectively in rare conditions (Mann 2003); and it is prone to prevalence-incidence bias especially in the case of long-lasting diseases (Levin 2006). Given that many outcomes were investigated in the present research and the advantages of a cross-sectional study, this design was used in the present study. In addition, since participant drop-outs may be associated with many visits, therefore, to avoid inadequate sample size, the design was chosen.

### **7.2.2 Sample Size Determination**

Following a pilot study with healthy children ( $n = 5$  healthy participants) (section 5.12), a power calculation was performed using an online computer programme 'Power and Sample Size Calculation' (PS 2005), to determine the sample size (at 90% power and  $\alpha = 0.05$ ) for this study. Sample size calculation was based on two independent group comparisons (assuming normality). No previous data was available on minimal clinically relevant difference in knee joint proprioception in children. However, during a discussion with an expert who had published extensively in the field of proprioception (R. J. Petrella, personal communication 02/02/2005), it was suggested that a mean difference of  $3^{\circ}$  could be used as the minimal clinically relevant difference in knee joint proprioception (JPS) between healthy children and those with HMS. A standard deviation of  $2.7^{\circ}$  was also used in the calculations (based on the pilot study in section 5.6.7). This indicated that 27 subjects were required in each group (healthy children and children with HMS).

A second power calculation was carried out after the repeatability experiments (section 6.2) with healthy children to confirm the sample size previously determined. Using the standard deviation of the repeatability study for the JPS test at  $25^{\circ}$  ( $n = 10$  healthy children) but all other factors remaining the same, revealed that 26 subjects were needed in each group to detect a statistically significant difference. Following these power calculations, it was decided by the researcher to recruit as many subjects as possible in each group to allow for sub-group analyses, account for potential attrition and enhance generalisability of the findings.

It has been suggested that when there is more than one outcome measure such as in the present study (joint proprioception, muscle torque, ROM, functional ROM, pain and QoL), the sample size for each outcome measures should be calculated and the result of the largest sample size from the calculations should be used for the study (Rigby and Vail 1998). This was not the case in the present study, however, because impaired joint proprioception may be a key factor associated with HMS. For example, impaired knee joint (Hall et al. 1995) and proximal interphalangeal joint (Mallik et al. 1994) proprioception has previously been observed in adult patients with HMS when compared with matched controls. Knee joint proprioception has also been reported to be impaired in subjects with generalised joint laxity (Barrack et al. 1983b). Therefore, it was considered that knee joint proprioception might also be affected in children diagnosed with HMS. Additionally, joint proprioception was the focus of the present research. Within the present study, two proprioception outcomes (knee joint kinaesthesia and joint position sense (at 25° and 10° knee flexion)) were examined. Comparisons of the results of the repeatability experiment in healthy children (section 6.4) revealed no significant difference ( $p$  range = 0.146 to 0.894) between knee joint kinaesthesia (JK) and joint position sense (JPS) tests (at 25° and 10° knee flexion). Additionally, no significant difference was observed between JPS at 25° and 10°. Given these reasons, a pragmatic decision was made by the present researcher to use the knee joint proprioception (JPS at 25°) as the outcome measure for power calculation in the present study.

### **7.2.3 Healthy Subjects Design**

HMS commonly affects children between the ages of 8 to 15 years (Finsterbush and Pogrund 1982; Biro et al. 1983). Gait maturation in children reaches its peak at the age of 8 years (Kato et al. 1993). In addition, the task undertaken during JPS and JK tests may be difficult to perform by children younger than 8 years, and generalised joint laxity (GJL) is known to decrease with increasing age (Cheng et al. 1991; Flynn et al. 2000; Jansson et al. 2004). Moreover, HMS is more common in girls than boys (Everman and Robin 1998; Vougiouka et al. 2000; Jasson et al. 2004; Sekin et al. 2005; Bird 2007) and varies among people of different ethnic origin. In order to create a database for comparison, a sample representing the HMS population, should, ideally, have a spread of age, gender and ethnic background. However, it was difficult to control for all these variables within a relatively small sample of children with HMS. Therefore, a database of a convenience sample of healthy children aged 8-15 years was chosen.



### **7.2.3.1 Ethical Considerations and Approval**

#### **General Ethical Codes**

There are two codes of ethics that provide guidance to physiotherapy researchers. The first code is the Nuremberg treaty that was developed in 1949 on permissible medical experiments (Levine 1988). It highlights 10 principles for the conduct of medical research. This code was moved forward in 1964 by the World Medical Association's Declaration of Helsinki that was modified in 1975 (Levine 1988). This provided 12 guiding principles for the conduct of research involving human subjects. The Helsinki Declaration provides international ethical guidance relating to research involving human subjects and supports the details contained within the Nuremberg Code and clarifies them. It also examines issues pertaining to children participating as subjects in research, for example informed consent. Both the Nuremberg and Helsinki documents are discussed in detail by Levine (1988).

#### **Ethical Considerations in Paediatric Research**

Ethical principles provide a basis for making decisions about professional and personal conduct. Research involving children is associated with some ethical issues that may not be encountered in competent adults (Puntney 2002). Greig and Taylor (1999) stated that there are challenging ethical dilemmas faced by researchers undertaking research with children and their families. Ethical issues in research involving children have recently been the subject of discussion (Greig and Taylor 1999). Therefore, ethics in relation to research with children requires the knowledge of both general ethics theory and exploration of the general principles of undertaking research on human subjects. The potential ethical issues in research involving children were carefully considered when planning and implementing the present research. In this section, the general ethical codes regarding the conduct of research involving human subjects are highlighted. The ethical issues in this study that are peculiar to research in children that are not commonly encountered with competent adults and how they were addressed are discussed below.

### **7.2.3.2 Ethical Considerations**

#### **Informed Consent (Voluntary)**

The Children (Scotland) Act (Scottish Executive 1995) stated that children under the age of 16 years may consent to treatment provided they have sufficient understanding of what is proposed. A child's ability to give informed consent depends on their lived experience or social context in terms of how much they understand what is involved in a research (Puntney 2002). As a result, it has been suggested that consent for treatment should be obtained from both the child and parent (Dimond 1996; Puntney 2002). Although consenting for treatment is not the same as giving consent for taking part in research, Dimond (1996) advocated that similar consideration should prevail. To ensure that the children knew that they had a choice as to whether to participate in the present study and that they had right to withdraw from the research at any time if they wished, informed written consent was obtained from both the healthy children and their parents or guardian (Appendix 3.6 and 3.7). Informed written consent was also obtained from children with HMS and their parents/guardians (Appendix 3.12 and 3.13). The present researcher explained the test procedure, duration of the study and verbal consent was also ongoing during the data collection process to develop trust between the researcher and children (Puntney 2002).

#### **Child Protection**

Children (Scotland) Act (Scottish Executive 1995) acknowledged that children can be victims of physical, sexual, and emotional abuse, neglect and bullying from adults working with them. Child abuse can have serious and long-term effects on all aspects of a child's health, development and well-being (DoH 1989). Sustained abuse is likely to have a deep effect on a child's self-image, self-esteem and future life (DoH 1989). Therefore, to ensure that the children that participated in the present research were protected, the following were considered.

A Disclosure Scotland check was obtained to ensure that the present researcher did not have any criminal record that prevented him from having contact with children. Disclosure Scotland is a service provided by Scottish Ministers to manage and operate in Scotland to provide informed decisions about people having contact with children or other vulnerable members of the society such as the elderly, sick, people with disabilities or special needs. The researcher did not have direct access to the

children involved in the research as they were approached through their parents or guardians. None of the participating children was examined by the researcher without their parent/guardian or an accompanying adult present during data collection.

#### **7.2.3.3 Ethical Approval**

Ethical Approval was applied for and granted by Queen Margaret University Ethics Committee (Appendix 3.8) and the Department of Education, Edinburgh City Council (Appendix 3.9) for access to all healthy school children and their participation in this study. Ethical approval was also granted by QMU (Appendix 3.8) and the Lothian Local Research Ethics Committees (Appendix 3.14) for the testing protocols and access to all patients with HMS. The parents of all participants (healthy and HMS) and the participants were not asked to consent to the study for at least 48 hours after receiving the information about the study. In accordance with the data protection act (1984), a coding procedure was adopted so that only the principal investigator knew which results pertained to which subject.

#### **7.2.3.4 Design (Healthy Subjects)**

In order to be able to generalise the findings of the present study and to allow for sub-group analysis, a convenience sample of thirty-seven healthy children volunteers were recruited (20 boys and 17 girls). Each group was further split into 2 age cohorts i.e. 8 to 12 years, and 13 to 15 years. In order not to disrupt the children's school activities and for the convenience of parents/guardians, healthy subjects were tested in the afternoons (after school), on Saturdays mornings and during school holidays.

#### **7.2.3.5 Recruitment and Exclusion Criteria**

Healthy school children were recruited between October 2004 and September 2005 and were drawn from the following populations:

- (1) Local Primary and Secondary Schools.
- (2) Children of staff members of Queen Margaret University, Edinburgh.

These populations were chosen as it was easier to arrange participants' visits to the University because the majority of the volunteers lived within the area. The potential participants (from schools) were identified by head teachers of the participating schools. A letter of invitation to participate in the study together with a response slip (Appendices 3.1 and 3.2) was sent by the head teachers of the participating schools

to the parents of all the potential participants. Parents that agreed for their children to participate in the research completed the response slip and returned it to the head teacher of their children's school. Following this, a letter of invitation, response sheet, pre-paid envelope, information sheet and copies of parental and participant consent forms (Appendices 3.3 to 3.7) were sent by the investigator to the parents that were willing to allow their children to participate. Parents were asked to return the completed response sheet and signed consent forms (one each) to the investigator in the pre-paid envelope. The response sheet contained the contact details of the participants.

On receiving the completed response sheet and consent forms, the investigator contacted the parents of the participants by telephone to confirm that they were still interested and to make necessary arrangements for the child and parent/guardian to visit the University. A letter of invitation was sent to parents of approximately two hundred healthy school children to ask if they would allow their children to participate in the study. Responses were received from 47 parents indicating their willingness to allow their child/children to take part in the study. Two participants were excluded (one with a severe knee injury within the last six months and another with multiple joint pain). Seven healthy children failed to turn up for testing. In total, 38 participants attended the laboratory to participate in the study. Of these 38, one participant changed her mind and withdrew before testing began, without giving any reason. This left 37 healthy children to participate in the investigation.

Recruiting healthy subjects was challenging for the following reasons:

- The researcher had no direct access to the school children.
  - Children were not seen without their parents or an adult accompanying them.
- As a result it was not easy to find suitable times to attend for testing.

On arriving at QMU, the parents and the participating children were received by the investigator at reception, from where they were led to the human motion analysis laboratory (HMAL). In the HMAL, the purpose and testing procedures of the study were restated and the children and parent/guardian were asked if they were still willing to participate. Each child and his or her parent/guardian were also given opportunity to ask questions regarding the testing procedure. At this point, the

timescale for the testing session was reiterated and the testing procedure commenced.

#### **7.2.4 HMS Subjects Design**

Twenty-nine children (8 boys and 21 girls) diagnosed with HMS aged 8 to 15 years were recruited from the rheumatology out patient department at the Royal Hospital for Sick Children (RHSC), Edinburgh and Springwell Podiatry Clinic, Edinburgh.

#### **Recruitment, Selection, Inclusion and Exclusion Criteria**

Suitable participants with HMS were initially identified using the medical record system of the rheumatology outpatient department at the RHSC, Edinburgh by a clinical specialist physiotherapist (the local investigator) at the hospital and the medical secretary at the rheumatology department. Patients were recruited from the medical case record of those that had a consultation within the previous 5 years (2000 to 2005).

The local investigator and medical secretary identified the potential participants under the terms of the ethical approval given by the Local Research Ethics Committee. They were also responsible for sending the letter of invitation (Appendix 3.10), signed by the Consultant rheumatologist, to the parents of the identified children. Recruitment was limited to consultations within the past 5 years because it was believed that the response rate might be poor if longer periods were used (for example, the families might have changed address). Additionally, the researcher felt that most patients were likely not to be within the age group (8 – 15 years) used for the study. Children diagnosed with HMS were also recruited from the Springwell Podiatry Clinic, Edinburgh. Due to a shortage of secretariat staff in this clinic, potential participants were identified from the previous patients' medical record system by the researcher. To do this, the researcher went through each case file of all patients seen at the clinic from January 2000 to September 2005. Patients aged 8 – 15 years diagnosed with HMS who fulfilled the inclusion criteria (as stated in the following section) were selected for inclusion in the study. The inclusion/exclusion criteria were established using the information available from the medical records of the participants.

A letter of invitation (Appendix 3.10) to participate in the research was also sent to the parents of the potential participants by the Head of Podiatry at Springwell Podiatry Clinic. Attached with the letters were a response sheet (Appendix 3.4), pre-paid envelope and information sheet (Appendix 3.11). Parents were asked to return the completed response sheets (to the investigator) in the pre-paid envelopes provided. The response sheet contained the contact details of the participants. It was emphasised on the letter that their participation in the research was not going to affect or alter any treatment.

On receiving the completed response slips, the investigator contacted the parents of the potential participants to confirm if they were still interested in taking part and to make necessary arrangements for their visit to the University. Parents of 103 children with HMS were contacted and responses were received from 36 parents (accounting for 35%), indicating their willingness to allow their children to take part in the study. However, letters delivered to the addresses of three (of the 103) potential participants were returned, as they were not known at the given address. Five subjects were excluded (3 with Ehler Danlos syndrome, 1 with rheumatoid arthritis, 1 with learning difficulty) while 2 subjects did not turn up for participation, leaving 29. All testing was carried out in the HMAL at QMU and the procedure was as described for healthy children in 7.3.3. Patients were recruited between July 2005 and October 2005.

Patients were difficult to recruit because the investigator did not have direct access to the medical record system. The investigator therefore relied on the local investigator and medical secretary to help identify patients. A limited number of patients were identified in this manner and it is possible that not all the parents of the eligible patients were contacted. Due to child protection law (Scottish Executive 1995), children were not seen without their parents or an accompanying adult. This made it difficult to arrange a suitable time for some participants and children to attend the laboratory.

### **Inclusion/ Exclusion Criteria**

The local investigator was asked to apply the following general inclusion/exclusion criteria to the potential participants, using the information available from the medical records:

1. Aged between 8 to 15 years. The reasons for choosing this age group have been discussed in section 7.2.3 of this thesis.
2. Subjects must have been diagnosed (based on the Beighton criteria) with HMS to be recruited to the HMS group.
3. A minimum Beighton score of 6/9.
4. Subjects must not show any evidence of identifiable hereditary disease of the connective tissue such as Marfan syndrome.
5. Subjects must not have cognitive difficulty and/or visual impairment. Cognitive difficulty may affect a child's ability to consent to the research as they may not be able to understand the study protocol, making their participation unethical (Puntney 2002).
6. Subjects with rheumatoid, juvenile idiopathic arthritis and other rheumatological disorders were excluded from participating. This was because these conditions may be associated with musculoskeletal complaints and poor quality of life (Jarwoski 1993; Schanberg et al. 2003; Sallfors et al. 2004).
7. Subjects with developmental coordination disorder were also to be excluded as muscle performance (Raynor 2001), perception deficits (Newnham and McKenzie 1993) and information processing problems (Raynor 1998) have been found in children with this condition.
8. Children (healthy or those with HMS) with an injury affecting the knee joint were also excluded as it is believed that this may cause impairment in joint proprioception.

Participants were still invited even where information regarding the above was not available. The presence of any of the above, with the exception of the Beighton score, was confirmed on the telephone with the parent/guardian of each participant before an appointment was made for their visit to the laboratory. Beighton score was confirmed by the researcher in HMAL before testing.

### **7.3 Procedure**

Each subject wore a T-shirt and a pair of lycra<sup>®</sup> shorts as this enabled the researcher to identify the bony landmarks at the knee joint. Demographic details including age, gender, height body weight, age of onset of HMS symptoms, joints affected and type of treatment received by the patients were collected. Lower limb dominance was also determined by asking each participant to kick a football to a target (Sadeghi et al. 2000; Wiggin et al. 2006). The details of the testing protocol have been presented in section 6.2. In addition to this, Beighton scores were used by the investigator to determine the extent of generalised joint laxity in children with HMS before testing. This was done to confirm the diagnosis and to allow exploration of the possible relationship between Beighton scores and the possible impairments, activity limitations and participation restrictions in children with HMS.

Patients with Beighton scores of 6/9 or more (Mikkelsen et al. 1996) were included in the study. A Beighton score of 6/9 was used because that was the cut-off point used by the Consultant rheumatologist at the RHSC, Edinburgh. The assessment method developed was used for assessing the level of neuromuscular impairments, functional ability and QoL in children with HMS.

In summary 37 healthy children (20 boys and 17 girls) and 29 children with HMS (8 boys and 21 girls) were included in the study.

### **7.4 Data Analysis**

#### **7.4.1 Test of Normality/Descriptive Statistics**

Tests of normality were performed with SPSS version 13 (SPSS, Chicago, IL, USA) using the Shapiro-Wilk tests (for samples  $\leq 50$ ). Normality tests revealed that some variables were normally distributed while some were not normally distributed (Appendix 3.15) in both healthy children and those with HMS. Non-normally distributed data was transformed with SPSS version 12 using log to base ten (Bland and Altman 1996b). Transformation of the data was attempted to enable the researcher to apply parametric statistical analysis, believed to be a more powerful statistical test than the non parametric statistically analysis (Morgan et al. 2004; Munro 2005). Following the process of transformation, however, only extension ROM attained normal distribution. The other non-normally distributed variables could



not be transformed. The transformed data was therefore not used. Parametric statistical analysis (independent t-test) was used to compare normally distributed data while the non parametric equivalent (Mann Whitney-U test) was used to compare the non-normally distributed data. There were instances where the data for either healthy children or HMS cohort were normally distributed and were non-normally distributed in the other group. Group comparisons for such data were also made using the Mann Whitney-U tests due to the occurrence of non-normally distributed data.

The mean and standard deviation of normally distributed data were calculated and reported for healthy children and children diagnosed with HMS (Morgan et al. 2004; Munro 2005). The median and interquartile range of non-normally distributed and ordinal variables were calculated and reported (Morgan et al. 2004; Munro 2005).

### **7.4.2 Inferential Statistics**

#### **Group Comparisons**

Normally distributed data (flexion ROM, kinematics data and muscle torque) (Morgan et al. 2004; Salkind 2004; Munro 2005) in healthy children were analysed using independent sample t-tests. However, Mann - Whitney U tests were performed for non-normally distributed (pain, extension ROM, JPS, JPS at 25<sup>0</sup>, JPS at 10<sup>0</sup>) and ordinal data (QoL) (Morgan et al. 2004; Salkind 2004; Munro 2005) in healthy children. Differences between healthy and HMS cohorts were examined using independent sample t-tests for normally distributed data (functional ROM). Similarly, Mann - Whitney U tests were applied to examine group differences for non-normally distributed (pain, ROM, muscle torque, kinaesthesia, JPS 25<sup>0</sup> and at 10<sup>0</sup>) and ordinal data (QoL) between healthy and HMS cohorts. Statistical significance was set at the 95% probability level ( $\alpha \leq 0.05$ ) (Morgan et al. 2004; Salkind 2004; Munro 2005).

#### **Relationships between Variables**

The relationships between the following variables were investigated using Spearman rho correlation coefficients: Knee JK and JPS tests in healthy children; pain and each of the measured variables in children with HMS; and Beighton scores and all the parameters included in the outcome measures used in the present study. Values of  $r > -0.5$  and  $> 0.5$  were accepted as high negative and positive correlation respectively (Morgan et al. 2004; Salkind 2004; Munro 2005). All correlation

analyses reported in this thesis are expressed using correlation coefficients ( $r$ ). Pain was used as the independent variable for correlation analysis because HMS is often diagnosed by the presence of generalised joint laxity and musculoskeletal pain (Mikkelsen et al. 1996; Ferrell et al. 2004). Moreover, clinicians believe that pain is a primary indicator in children with HMS (Everman and Robin 1998; Gurley-Green 2001; Murray and Woo 2001).

The results of neuromuscular, functional ROM and QoL in healthy children, those with HMS and the comparisons of the two groups are reported in the next section.

## **7.5 Results**

Sixty-six children (37 healthy and 29 with HMS) participated in this study. Neuromuscular performance, functional ROM during walking and QoL characteristics were determined. Raw data for these measurements in healthy children and those with HMS is provided on a CD-ROM (Appendix 5). To fulfil the primary and secondary aims of the study, data analyses were carried out to investigate the following:

- The differences between healthy children and those with HMS.
- The relationships between pain and each of the following: neuromuscular impairments, activity limitations and participation restrictions in children with HMS.
- The relationships between Beighton scores and all the outcomes measured in children with HMS.
- Gender- and age-related patterns on these variables in healthy children.
- The relationships between joint kinaesthesia (JK) and joint position sense (JPS) tests in healthy children.

The results of these analyses are presented in this section.

### **7.5.1 Subject Demographics**

The healthy children cohort consisted of 20 boys and 17 girls. The HMS cohort comprised of 8 boys and 21 girls diagnosed with HMS based on the Beighton scores. Table 7.1 shows the mean and standard deviation (SD) age, height and weight of the healthy and HMS children. Table 7.2 presents the average Beighton scores and age of onset of symptoms in children diagnosed with HMS. The average Beighton scores in boys and girls with HMS were similar. The mean age of onset of

pain recorded in boys with HMS was  $6.2 \pm 3.5$  years and was  $8.0 \pm 2.7$  years in girls with HMS. The combined average age of onset in children with HMS was  $7.5 \pm 3.0$  years.

The distribution of GJL in children diagnosed with HMS is illustrated in Figure 7.1. The Figure shows that laxity of the knee and elbow joints were the most common while forward flexion was the least common in children with HMS. The pattern of symptomatic (painful) joints in patients with HMS is demonstrated in Figure 7.2. From Figure 7.2, it can be seen that knees were mostly symptomatic in children with HMS and accounted for 86.2% of the HMS patients tested. Ankles were the next most symptomatic. The toes and elbow joint were found to be the least symptomatic in these children.

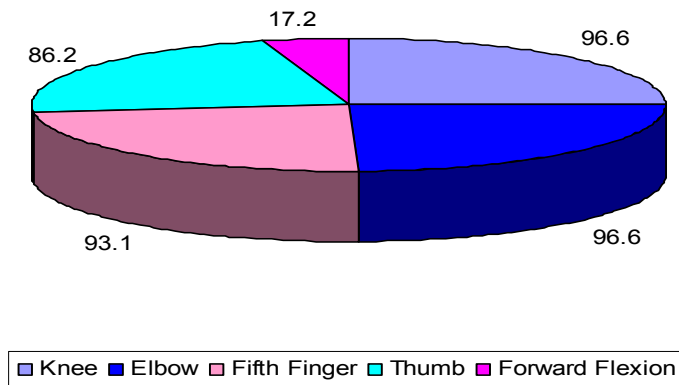
**Table 7.1: Characteristics of healthy children and those with HMS**

Cohort	Healthy Children (n = 37)		HMS (n = 29)		P values
	Mean	SD	Mean	SD	
Age (years)	11.5	2.6	11.9	1.8	0.482
Height (cm)	153.0	16.0	152.0	15.0	0.814
Body Mass (kg)	48.3	14.3	51.7	17.3	0.386
Activity level (hrs/week)	5.8	2.5	6.1	4.5	0.740

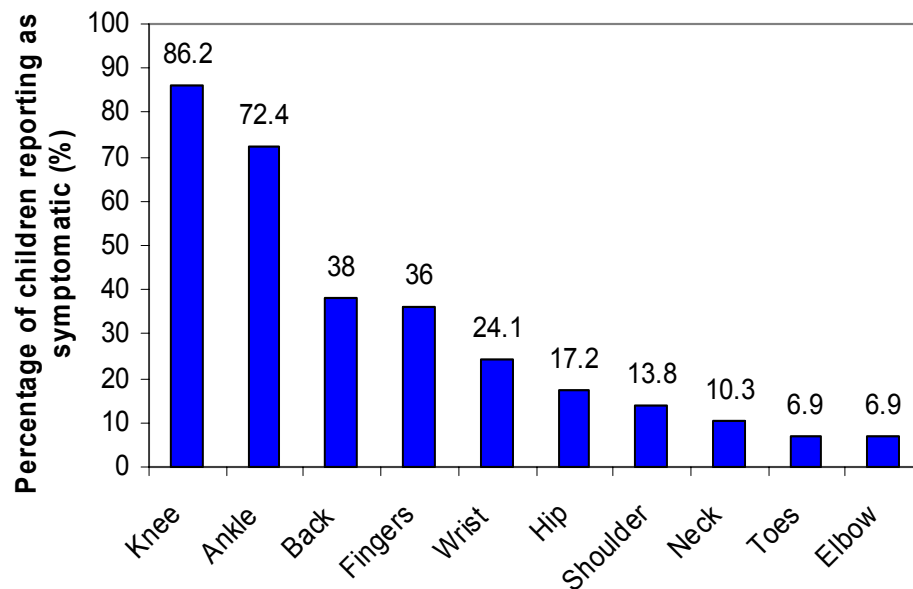
p values derived from independent t-test

**Table 7.2: Mean Beighton scores ( $\geq 6$ ) and age of onset of symptoms in children diagnosed with HMS**

Gender	Boys (n = 8)		Girls (n = 21)		All Subjects (n = 29)	
	Mean	SD	Mean	SD	Mean	SD
Beighton Scores	6.9	1.4	7.1	1.1	7.0	1.2
Age of onset of symptom	6.2	3.5	8.0	2.7	7.5	3.0



**Figure 7.1: Distribution of generalised joint laxity in children diagnosed with HMS (n = 29). Both the knee and elbow were mostly affected by joint laxity. The values shown are in percentage (%).**



**Figure 7.2: Pattern of symptomatic (painful) joints in HMS subjects (n = 29).**

### 7.5.2 Comparisons of Results of Healthy and HMS Children Cohorts

In order to identify differences between healthy and HMS children, all measurement variables were compared between healthy children and those with HMS using independent t-tests and Mann Whitney-U tests. The summary of the results are presented in Table 7.3.

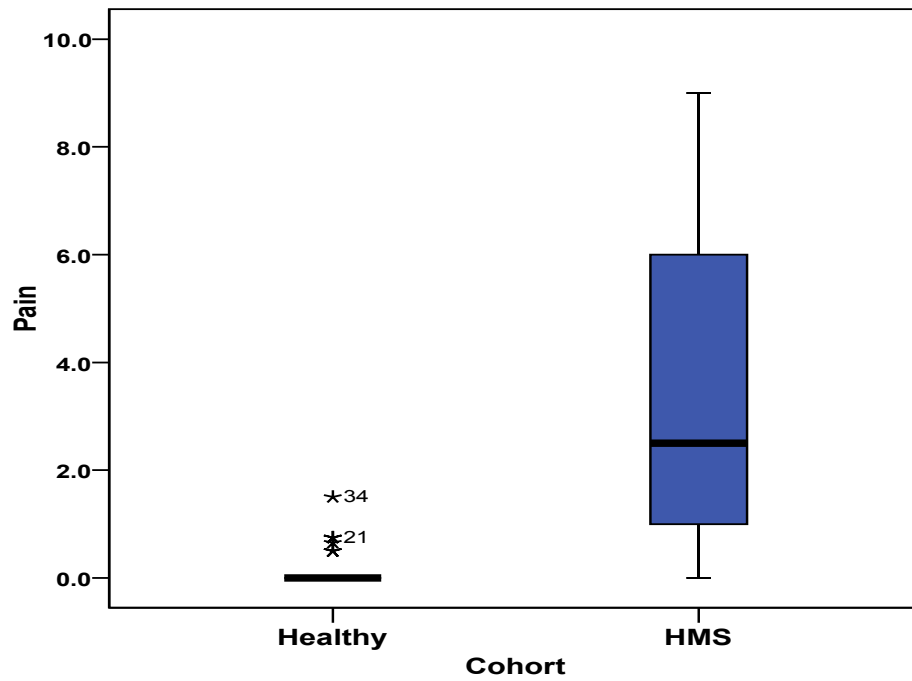
**Table 7.3: Mean (SD)/median (IQR) of measurements and p values in healthy children (n = 37) and children with HMS (n = 29)**

Variables	Healthy (n =37)	HMS (n =29)	p Values
Proprioception ( <sup>0</sup> )			
JK	2.0 (1.0)	2.0 (1.5)	<b>&lt;0.001*</b>
JPS at 25 <sup>0</sup>	3.0 (3.0)	7.4 (6.5)	<b>&lt;0.001*</b>
JPS at 10 <sup>0</sup>	1.0 (3.0)	6.0 (5.0)	<b>&lt;0.001*</b>
Muscle Torque (Nm/kg)			
Extension	1.5 (0.5)	1.2 (0.3)	<b>&lt;0.001*</b>
Flexion	0.8 (0.2)	0.6 (0.2)	<b>&lt;0.001*</b>
ROM( <sup>0</sup> )			
Extension	-4.0 (1.5)	-13.0 (3.0)	<b>&lt;0.001*</b>
Flexion	143.0 (4.5)	155.0 (5.5)	<b>&lt;0.001*</b>
Sagittal Knee Motion ( <sup>0</sup> )			
Extension	4.2 (6.0)	-1.0 (3.5)	<b>&lt;0.001†</b>
Knee Flexion LDR	20.0 (6.1)	12.6 (4.7)	<b>&lt;0.001†</b>
Max Knee Flexion	60.4 (6.6)	53.5 (4.6)	<b>&lt;0.001†</b>
Walking speed (m/s)	1.2 (0.4)	1.2 (0.1)	0.496†
Pain	0.0 (0.0)	2.5 (5.3)	<b>&lt;0.001*</b>
QoL			
Physical Functioning	100.0 (3.1)	75.1 (26.6)	<b>&lt;0.001*</b>
Emotional Functioning	100.0 (10.0)	90.0 (27.5)	<b>0.003*</b>
Social Functioning	100.0 (5.0)	90.0 (25.0)	<b>&lt;0.001*</b>
School Functioning	100.0 (0.0)	90.0 (45.0)	<b>0.008*</b>
Overall QoL	100.0 (6.8)	82.6 (21.8)	<b>&lt;0.001*</b>

†Values are in mean (SD) and by independent t-test, \*values in median (IQR) and by Mann-Whitney U test. Significant p values are indicated in boldface.

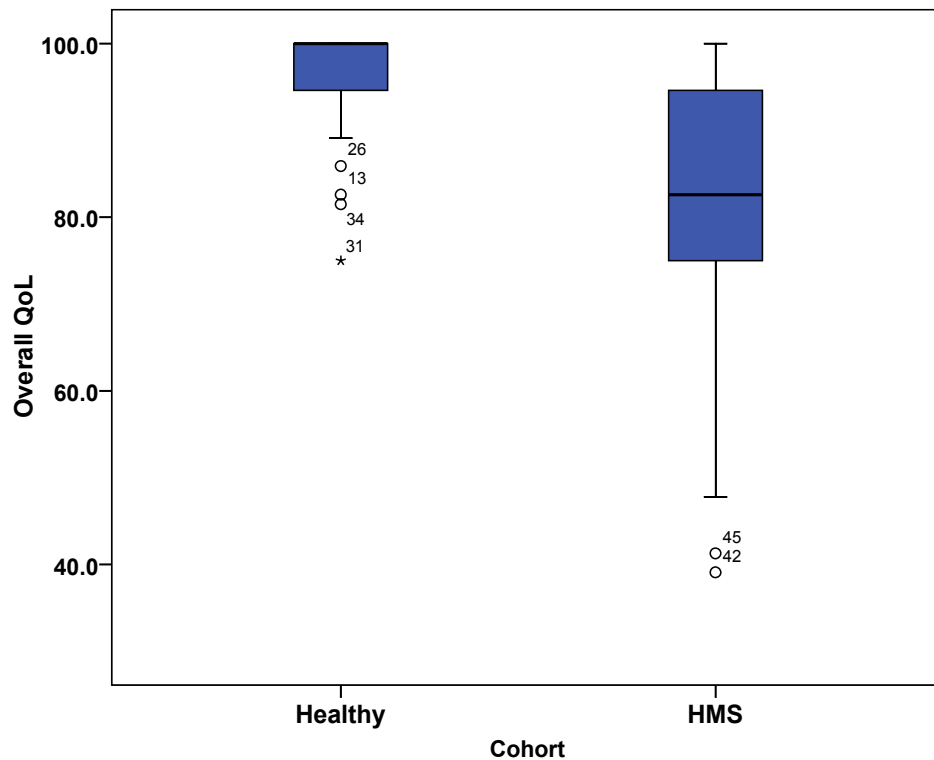
From the Table, it can be seen that there were significant differences ( $p$  range =  $<0.001$  to  $0.08$ ) between healthy children and those with HMS for all the variables measured except for walking speed ( $p = 0.496$ ). Figures 7.3 – 7.8 illustrate the median and IQR of pain, QoL, JK and AAE for the JPS measurements in healthy children and children with HMS. Figures 7.9 and 7.10 display the median and IQR of knee extensors and flexors muscle torque in healthy children and children with HMS in that order. In addition, the median and IQR of extension and flexion ROM in healthy children and children with HMS are demonstrated in Figures 7.11 and 7.12 respectively. The mean knee joint angles in sagittal plane during walking in healthy and HMS cohorts are shown in Figure 7.13.

From these box plots, the blue boxes represent the interquartile range (IQR) with the black line representing the median values. The whiskers represent the highest and lowest values excluding the outliers, which are represented with a small circle. Outliers indicate any values between the IQR box lengths from the upper or lower edges of the range and extremes (represented by a small star and indicating any values more than 3 IQR box lengths from the upper or lower edges of the IQR). Figure 7.3 shows the box plots for pain. From the Figure, it can be seen that the HMS cohort attained a higher median score than the healthy controls. There was no overlap of the IQR between healthy and HMS cohorts. There was a significant difference ( $p < 0.001$ ) between the median scores of pain between the two groups. This indicates that children with HMS experienced more pain than the healthy group.



**Figure 7.3: Box plots of pain in healthy children (n = 37) and children with HMS (n = 29)**

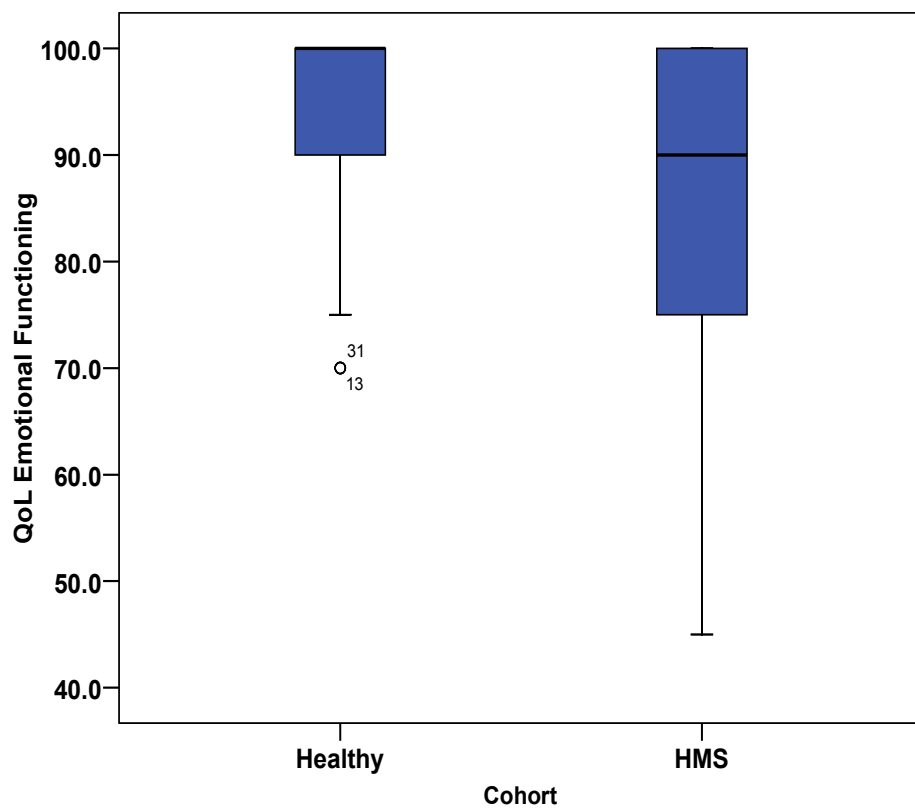
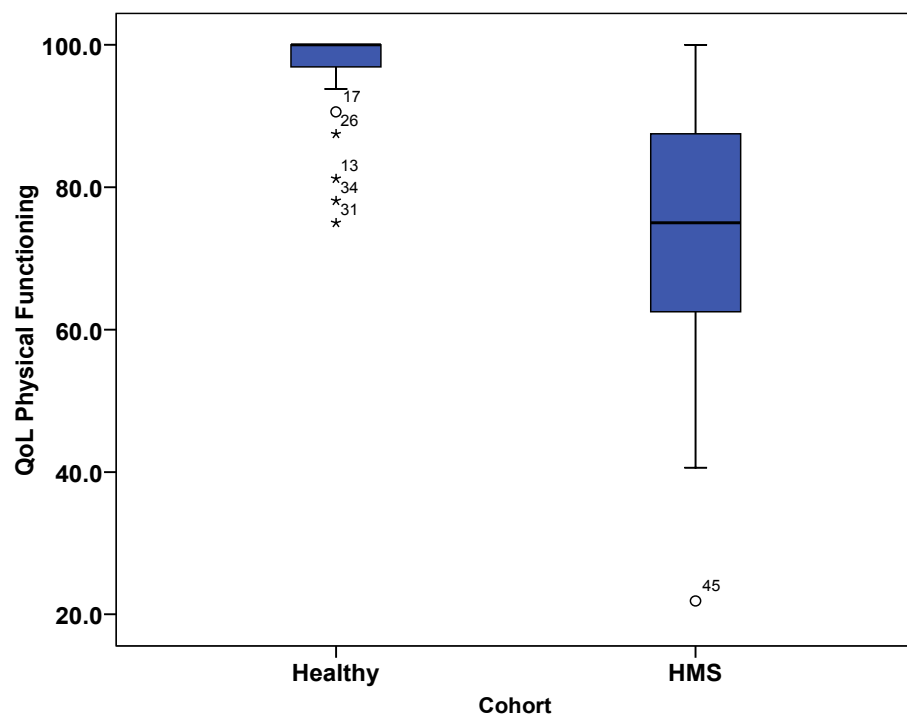
The box plots of the overall QoL perception is displayed in Figure 7.4. The Figure demonstrates higher median score in the overall QoL in children with HMS than the controls. QoL scores in the HMS group were widely spread while the healthy control had less variation. A statistically significant difference ( $p < 0.001$ ) was found in the overall QoL scores between the two cohorts. These results imply that healthy children had better QoL perception than those with HMS.

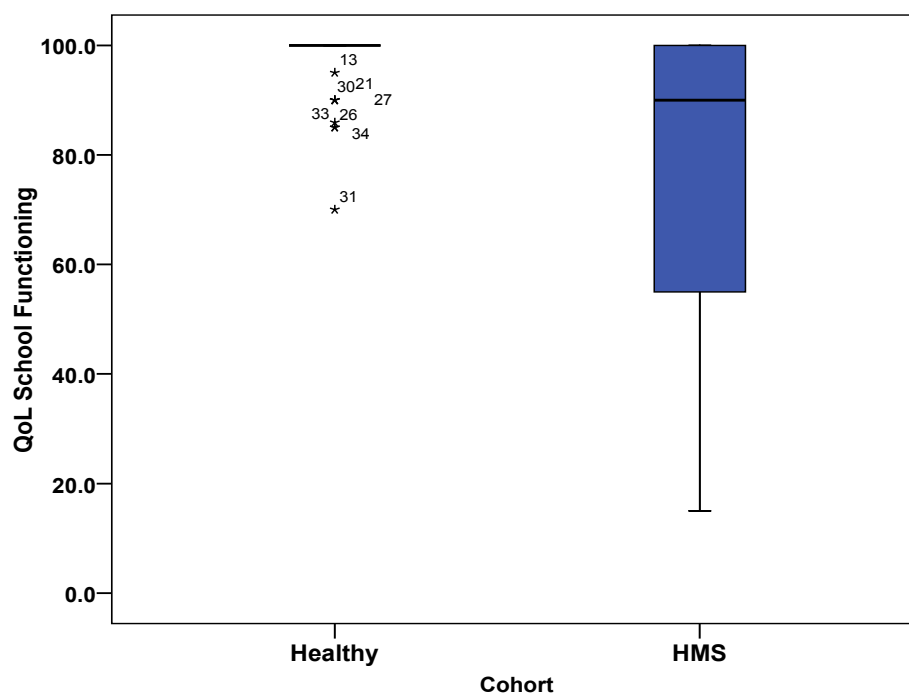
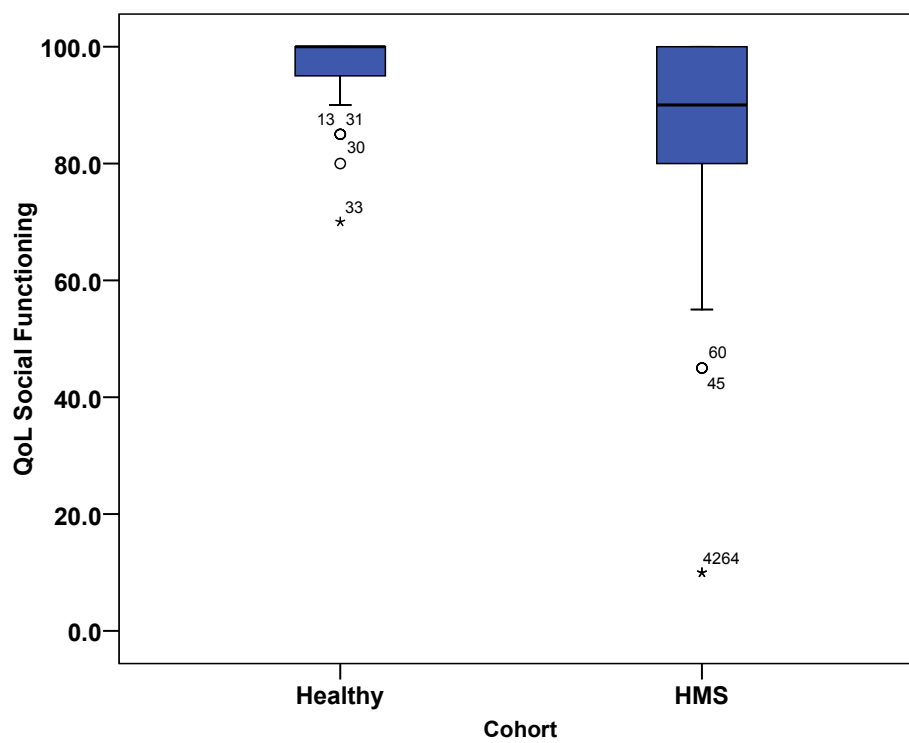


**Figure 7.4: Box plots of QoL in healthy children (n = 37) and children with HMS (n = 29)**

The median scores of QoL for the different domains are shown in Figure 7.5. It can be observed from the Figure, that the HMS cohort had higher median values of QoL in all the domains than the controls. The Figure also revealed that QoL scores for the HMS group were widely spread, while the controls displayed a relatively smaller amount of variation. There were significant differences (all  $p < 0.05$ ) in all the domains of QoL between the two groups. These findings show that healthy children had better QoL perception in physical functioning, emotional functioning, social functioning and school functioning than the HMS cohort.

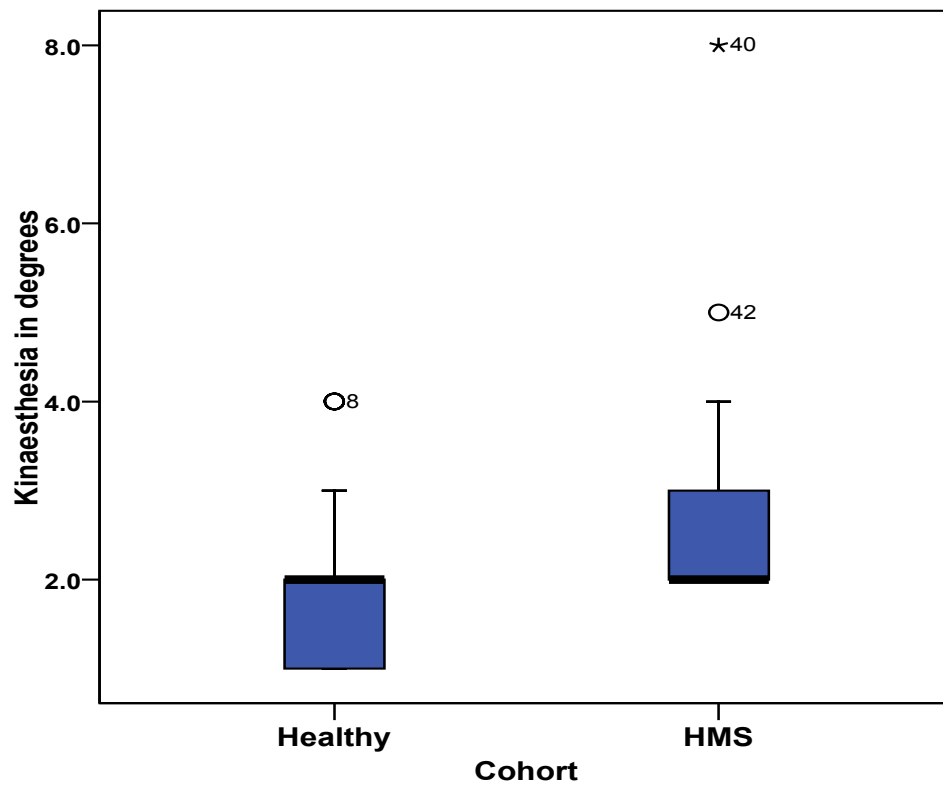






**Figure 7.5: Box plots of different domains of QoL in healthy children (n = 37) and children with HMS (n = 29)**

The box plots of JK and JPS tests are presented in Figures 7.6 – 7.8. The HMS group had higher median values of JK and AAE during JPS tests than healthy children. Significant differences ( $p < 0.001$ ) were found in JK and JPS measurements between the two groups. This signifies that knee JK and JPS were impaired in children with HMS compared with the healthy cohort.



**Figure 7.6: Box plots of JK in healthy children (n = 37) and children with HMS (n = 29)**

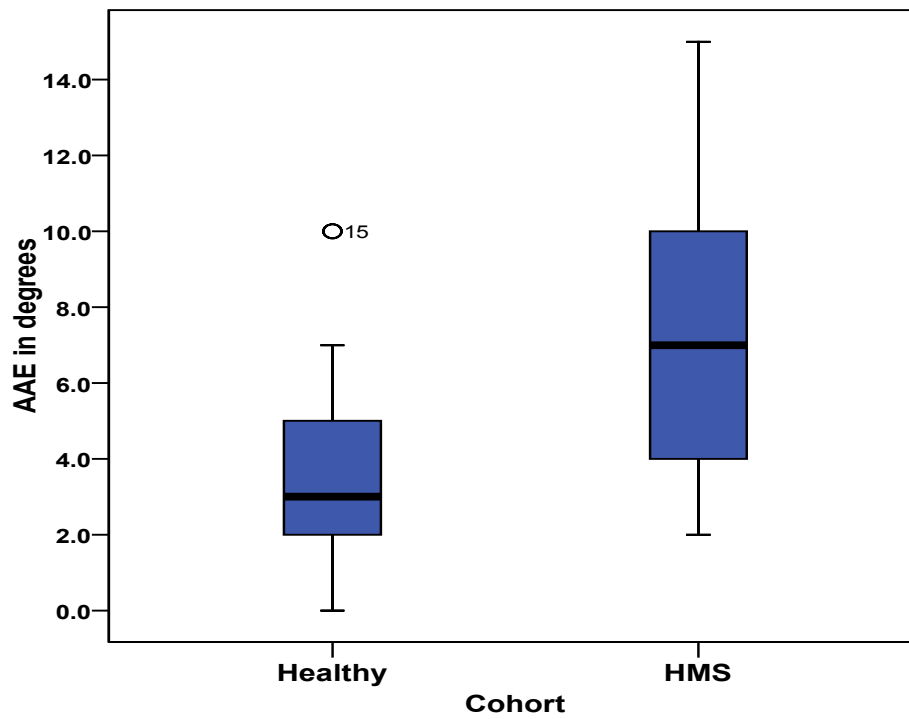


Figure 7.7: Box plots of JPS at 25° in healthy children (n = 37) and children with HMS (n = 29)

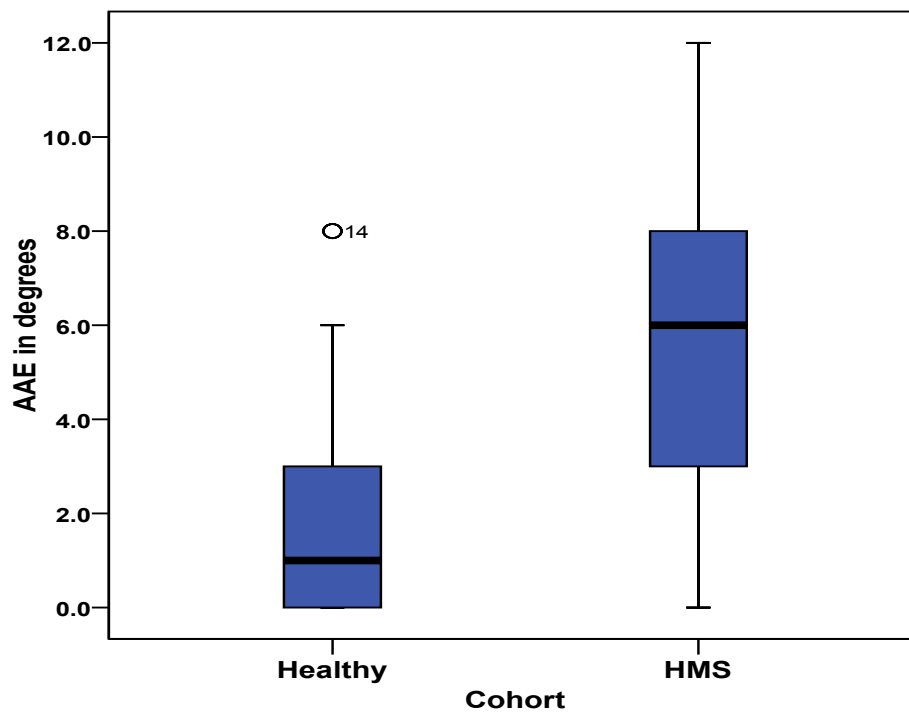


Figure 7.8: Box plots of JPS at 10° in healthy children (n = 37) and children with HMS (n = 29)

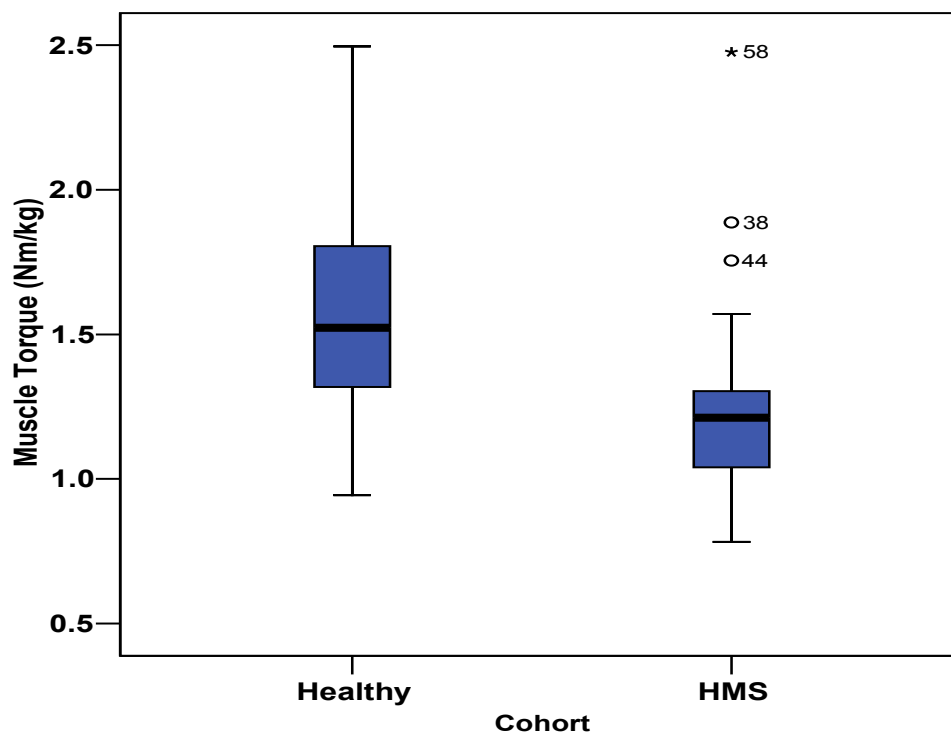


Figure 7.9: Box plots of knee extensors muscle torque in healthy children (n = 37) and children with HMS (n = 29)

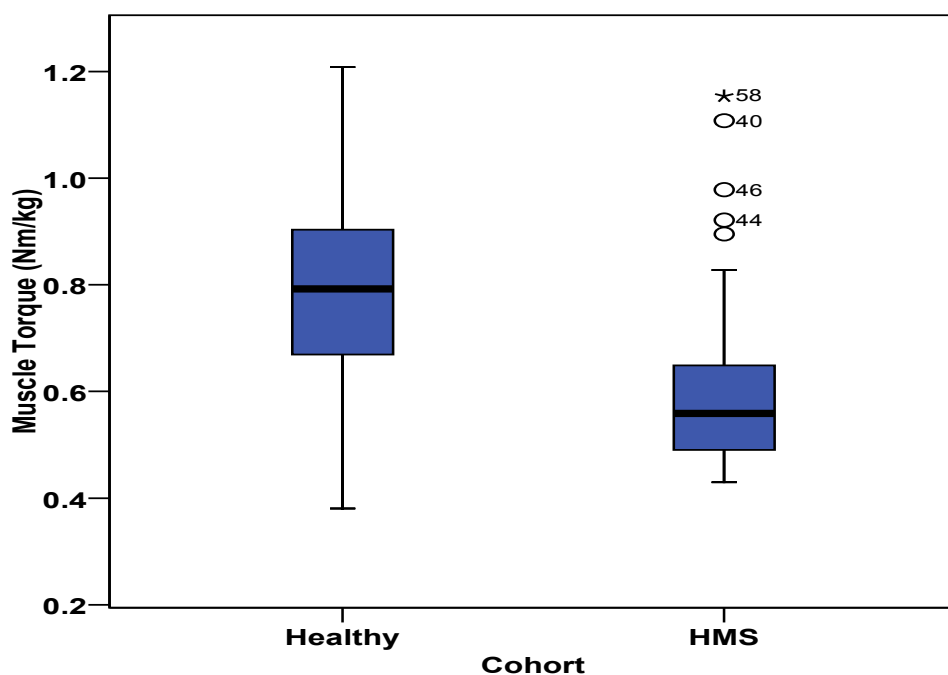
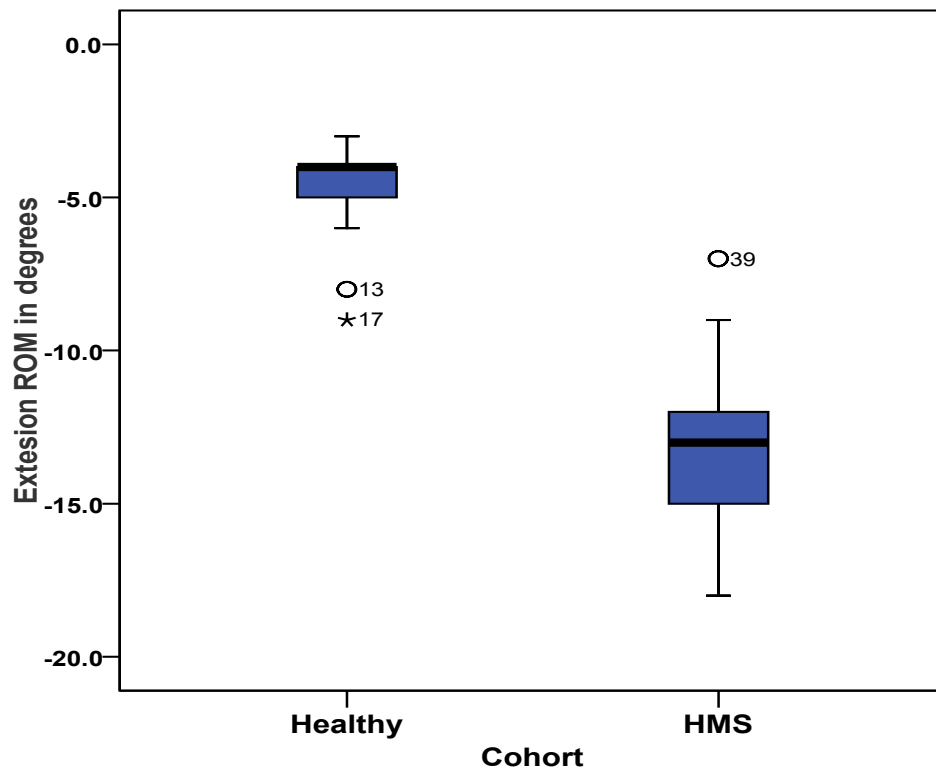
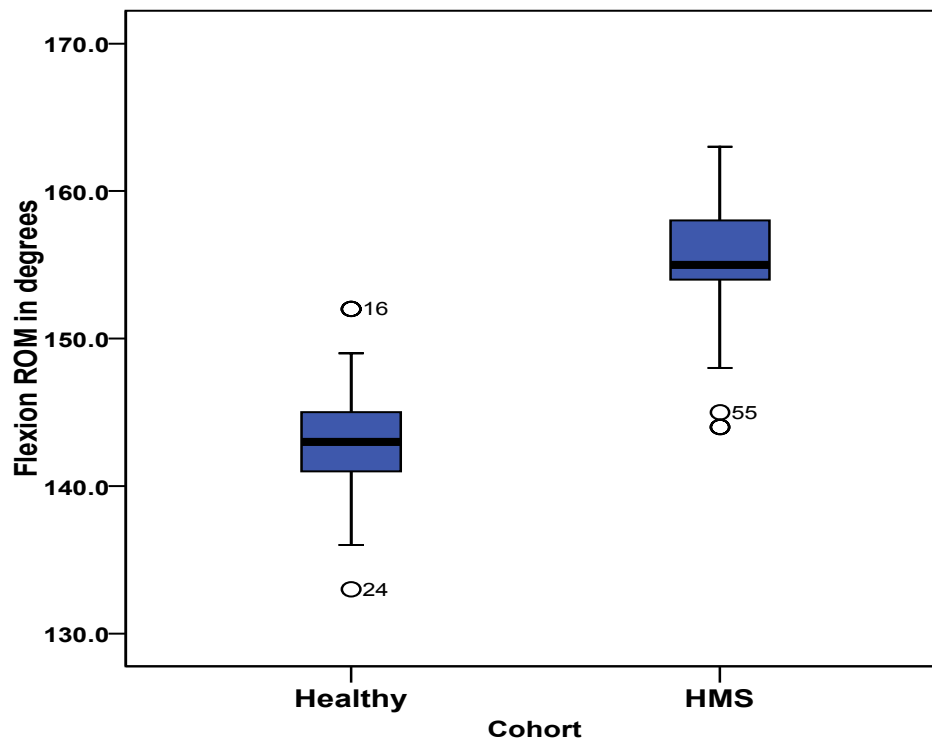


Figure 7.10: Box plots of knee flexors muscle torque in healthy children (n = 37) and children with HMS (n = 29)

Figures 7.9 and 7.10 depict the box plots of knee extensors and flexors muscle torque (in the controls and HMS cohort) respectively. Both the extensors and flexors muscle torque were significantly (both  $p < 0.001$ ) higher in healthy children than the HMS cohort. This implies that children with HMS exhibited weaker extensors and flexors muscle muscles than their healthy counterparts.



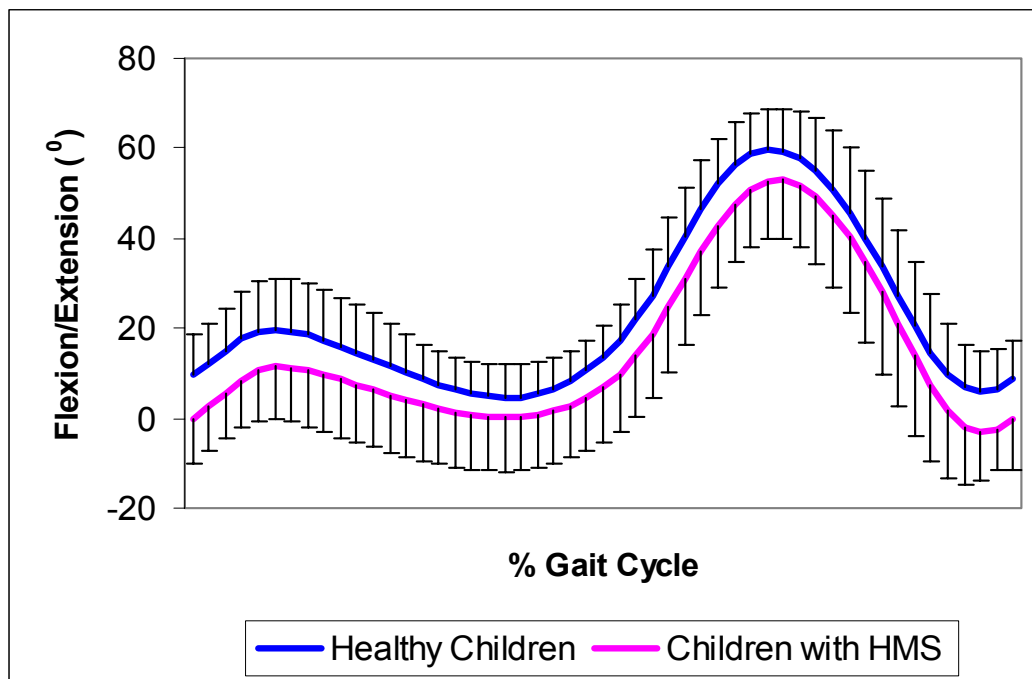
**Figure 7.11: Box plots of extension ROM in healthy children (n = 37) and children with HMS (n = 29)**



**Figure 7.12: Box plots of flexion ROM in healthy children (n = 37) and children with HMS (n = 29)**

The median values of knee extension and flexion ROM are displayed in Figures 7.11 and 7.12 respectively. These Figures demonstrate that the values of extension and flexion ROM were higher in children with HMS than in healthy controls. There were significant differences in extension and flexion (both  $p < 0.001$ ) ROM between the two groups. These findings imply that children with HMS had higher knee ROM than healthy children.

The mean knee angles in the sagittal plane during walking in the two groups are shown in Figure 7.13. It can be seen from the figure that knee extension in mid-stance, knee flexion during loading response and maximum knee flexion were higher in healthy children than in the HMS cohort. There were significant differences (all  $p < 0.001$ ) in knee joint angles in sagittal plane during walking between the two groups. These findings indicate that sagittal knee motion was lower in children with HMS than the controls.



**Figure 7.13: Mean ( $\pm 2SD$ ) knee angles in sagittal plane during walking in healthy children ( $n = 37$ ) and children with HMS ( $n = 29$ ). Error bars for healthy children = 2 (+SD) and error bars for HMS = 2 (-SD).**

In summary, children with HMS were found with significantly higher JK and JPS errors compared with the healthy controls. The HMS group also had significantly higher pain perception, passive ROM and knee extension during mid stance than the healthy cohort. However, muscle torque, knee flexion during walking and QoL scores were significantly lower in children with HMS than their healthy counterparts. These findings indicate that children with HMS exhibited neuromuscular impairments and abnormal gait patterns than healthy controls. These children also had poorer overall QoL (all the domains) than the controls.



### **7.5.3 Relationship between Pain, Neuromuscular Impairments, Activity Limitations and Participation Restrictions in Children with HMS**

Section 7.5.2 demonstrates the features associated with HMS in children. Pain in the presence of GJL is an index often used for diagnosing HMS (Engelbert et al. 2005; 2006). It is the most frequently reported neuromuscular impairment in these children (Everman and Robin 1998; Adib et al. 2005).

In order to examine the relationships between neuromuscular impairments, activity limitations and participation restrictions in children with HMS, correlation analyses were carried out between pain and each of the following: JK, JPS, muscle torque, passive ROM, functional ROM during walking and QoL. The data for pain was not normally distributed (Shapiro-Wilk test;  $p < 0.05$ ) and therefore a non-parametric correlation (the Spearman's rho correlation) was used. The summary of the correlations between pain and these measurement variables are presented in Table 7.4.

There was no statistically significant correlation between any of the variables, except for a moderate negative correlation between pain and overall QoL ( $r = -0.650$ ;  $p = <0.001$ ). There were also moderate to high negative correlations ( $r$  range =  $-0.479$  to  $-0.717$ ;  $p$  range =  $<0.001$  to  $0.009$ .) between pain and school, emotional and physical functioning domains of QoL in these children.

These findings indicate that using only pain as an index of diagnosis in conjunction with Beighton scores in children with HMS may not reflect the presence and level of other neuromuscular impairments such as proprioception and muscle torque in children with this condition. In addition, it seems that pain assessment alone may not indicate the extent of functional ROM in children with HMS. The significant correlation between pain and QoL in children with HMS signifies that a moderate relationship exists between these variables. This suggests that the higher the pain experienced by the children with HMS the poorer their QoL.

**Table 7.4: Spearman's correlations between pain, neuromuscular impairments, functional ROM during walking and QoL in children with HMS (n =29)**

<b>Variable</b>	<b>r Values</b>	<b>p Values</b>
Pain and JK	0.271	0.156
Pain and JPS at 25 <sup>0</sup>	0.071	0.715
Pain and JPS at 10 <sup>0</sup>	0.198	0.303
Pain and Extension Muscle Torque	-0.065	0.736
Pain and Flexion Muscle Torque	-0.118	0.542
Pain and KMST	-0.308	0.106
Pain and KFLRSP	-0.048	0.805
Pain and MKF	0.174	0.985
Pain and Overall QoL	-0.650	<b>&lt;0.001</b>
Pain and Physical Functioning (QoL)	-0.717	<b>&lt;0.001</b>
Pain and Emotional Functioning (QoL)	-0.614	<b>0.001</b>
Pain and Social Functioning (QoL)	-0.395	0.034
Pain and School Functioning (QoL)	-0.479	0.009

r = Spearman correlation coefficient: statistically significant values at  $\alpha < 0.0039$  (Bonferroni correction due to multiple correlations =  $0.05/13$ ) are indicated in boldface.

### 7.5.4 Results of Neuromuscular Performance, Functional ROM and QoL Characteristics of the Healthy Children Cohort

The level of neuromuscular, functional ROM and QoL characteristics in healthy children was examined. The summary of the results of all the measurement parameters in healthy children are shown in Table 7.5. Based on the results of tests of normality (Appendix 3.15), the mean/standard deviation (SD) of the normally distributed data and median/interquartile range (IQR) values of non-normally distributed data are reported as appropriate.

**Table 7.5: Mean/median and SD/IQR of all measurements in healthy children (n = 37)**

Variables	Mean	SD	Median	IQR
Proprioception ( $^{\circ}$ )				
JK	-	-	2.0	1.0
JPS at 25 $^{\circ}$	3.8	2.6	-	-
JPS at 10 $^{\circ}$	-	-	1.0	3.0
Muscle Torque (Nm/kg)				
Extension	1.6	0.3	-	-
Flexion	0.8	0.2	-	-
ROM( $^{\circ}$ )				
Extension	-	-	-4.0	1.5
Flexion	142.8	4.1	-	-
Sagittal Knee Motion ( $^{\circ}$ )				
Extension	4.2	5.6	-	-
Knee Flexion LDR	20.0	6.1	-	-
Max Knee Flexion	60.4	6.6	-	-
Pain	-	-	0.0	0.0
QoL (Functioning)				
Physical	-	-	100.0	3.1
Emotional	-	-	100.0	10.0
Social	-	-	100.0	5.0
School	-	-	100.0	0.0
Overall QoL	-	-	100.0	6.8

### 7.5.5 Effect of Gender on Neuromuscular, Functional ROM and QoL Characteristics in Healthy Children

In order to investigate the effect of gender, independent t-tests and Mann-Whitney U tests were carried out. Table 7.6 presents the summary of the results of healthy boys and girls.

**Table 7.6: Mean (SD)/median (IQR) of measurements and p values of differences between healthy boys and girls**

Variables	Boys (n =20)	Girls (n = 17)	p Values
Proprioception ( <sup>0</sup> )			
JK	1.0 (2.0)	2.0 (1.0)	0.122*
JPS at 25 <sup>0</sup>	3.3 (2.1)	4.5 (3.0)	0.138†
JPS at 10 <sup>0</sup>	1.0 (2.8)	1.0 (5.0)	0.582*
Muscle Torque (Nm/kg)			
Extension	1.6 (0.3)	1.6 (0.3)	0.906†
Flexion	0.8 (0.2)	0.8 (0.2)	0.624†
ROM( <sup>0</sup> )			
Extension	-4.0 (1.8)	-5.0 (2.0)	<b>0.020*</b>
Flexion	141.3 (3.8)	144.5 (3.9)	<b>0.015†</b>
Sagittal Knee Motion ( <sup>0</sup> )			
Extension	5.33 (4.1)	2.9 (7.5)	0.242†
Knee Flexion LDR	20.2 (4.6)	19.8 (7.6)	0.856†
Max Knee Flexion	59.9 (5.9)	61.1 (7.5)	0.568†
Pain	0.0 (0.0)	0.0 (0.3)	0.319*
QoL (Functioning)			
Physical	100.0 (0.0)	100.0 (7.8)	<b>0.022*</b>
Emotional	100.0 (7.5)	100.0 (10.0)	0.740*
Social	100.0 (5.0)	100.0 (7.5)	0.659*
School	100.0 (0.0)	100.0 (2.5)	0.453*
Overall QoL	100.0 (3.0)	98.9 (9.0)	0.410*

†Values are mean (SD) and by independent t-test, \*values are median (IQR) and by Mann Whitney- U test. Significant p values are indicated in boldface.

In the Table (7.6), it can be seen that the results for boys and girls are similar for all the outcomes. No significant difference was found between boys and girls in any variables measured except for extension ROM ( $p = 0.020$ ), flexion ROM ( $p = 0.015$ ) and physical functioning domain of QoL ( $p = 0.022$ ).

Therefore, separate ROM and physical functioning domain data may be required for healthy boys and girls.

The following section presents the results of the influence of age on the measurement parameters in healthy children.

#### **7.5.6 Effect of Age on Neuromuscular Performance, Functional ROM and QoL in Healthy Children**

The influence of age on neuromuscular, functional ROM and QoL indices in healthy children was investigated using independent t-tests and Mann Whitney-U tests. Regression analysis is commonly used for normally distributed data to determine the effect of one variable on another (Morgan et al 2004). However, since majority of the variables examined in the present study were not normally distributed Mann Whitney- U tests were used instead in to investiage the influence of age on neuromuscular performance, functional ROM and QoL. The results are shown in Table 7.7.

From Table 7.7, the results of these outcome measures are similar between younger children (aged 8 – 12 years) and teenagers (aged 13 – 15) except for JK, extension ROM, pain and QoL measures (overall QoL, emotional, social and school functioning) (all  $p < 0.05$ ). In most cases, there was a tendency that teenage children scored lower than their younger counterparts in all the measurements parameters. Due to the small sample size in each gender cohort and to minimise type I error the effect of age across each gender could not be investigated further by means of inferential statistics. However, descriptive statistics were carried out to reflect the possible pattern of all the outcomes across the two gender cohorts in healthy children. These are displayed in Table 7.8.

**Table 7.7: Mean (SD)/median (IQR) of measurements and p values of differences between healthy young children and teenagers**

<b>Variables</b>	<b>Young Children (n = 20)</b>	<b>Teenagers (n = 17)</b>	<b>p Values</b>
Proprioception ( <sup>0</sup> )			
JK	2.0 (1.0)	1.0 (1.0)	<b>&lt;0.001*</b>
JPS at 25 <sup>0</sup>	4.3 (2.5)	3.3 (2.7)	0.138†
JPS at 10 <sup>0</sup>	2.0 (3.8)	1.0 (2.0)	0.361*
Muscle Torque (Nm/kg)			
Extension	1.4 (0.3)	1.8 (0.3)	0.906†
Flexion	0.7 (0.2)	0.9 (0.2)	0.623†
ROM( <sup>0</sup> )			
Extension	-5.0 (1.8)	-4.00 (1.0)	<b>0.002*</b>
Flexion	144.5 (3.8)	140.8 (3.7)	0.906†
Sagittal Knee Motion ( <sup>0</sup> )			
Extension	5.1 (5.9)	3.2 (6.9)	0.218†
Knee Flexion LDR	19.7 (6.9)	20.4 (5.2)	0.856†
Max Knee Flexion	61.5 (7.2)	59.2 (5.8)	0.568†
Pain	0.0 (0.00)	0.00 (0.6)	<b>0.004*</b>
QoL (Functioning)			
Physical	100.0 (0.0)	100.0 (7.8)	0.052*
Emotional	100.0 (7.5)	100.0 (10.0)	<b>0.003*</b>
Social	100.0 (5.0)	100.0 (7.5)	<b>0.015*</b>
School	100.0 (0.0)	100.0 (2.5)	<b>0.002*</b>
Overall QoL	100.0 (3.0)	98.9 (9.0)	<b>0.013*</b>

†Values are in mean (SD) and by independent t-test, \*values in median (IQR) and by Mann Whitney- U test. Significant p values are indicated in boldface.

**Table 7.8: Mean (SD)/median (IQR) of measurements in healthy children by age and gender**

<b>Variables</b>	<b>Young Boys (n = 10)</b>	<b>Young Girls (n = 10)</b>	<b>Teenage Boys (n = 10)</b>	<b>Teenage Girls (n = 7)</b>
Proprioception ( <sup>0</sup> )				
* JK	2.0 (1.3)	2.0 (1.3)	1.0 (0.0)	2.0 (1.0)
†JPS at 25 <sup>0</sup>	3.5 (1.4)	5.1 (3.1)	3.0 (2.6)	3.7 (3.0)
*JPS at 10 <sup>0</sup>	1.5 (3.0)	2.0 (5.3)	1.0 (2.0)	1.0 (5.0)
Muscle Torque (Nm/kg)				
†Extension	1.5 (0.3)	1.3 (0.3)	1.7 (0.4)	1.8 (0.1)
†Flexion	0.8 (0.2)	0.69 (0.2)	0.8 (0.2)	0.9 (0.8)
ROM( <sup>0</sup> )				
*Extension	-4. 6 (1.0)	-5.0 (1.8)	-3.0 (1.00)	-4.0 (3.0)
†Flexion	142.9 (2.3)	146.1 (4.3)	139.7 (4. 5)	142.3 (1.4)
Sagittal Knee Motion ( <sup>0</sup> )				
†Extension	7.1 (2.9)	3.0 (7.5)	3.5 (4.5)	2.7 (8.1)
†Knee Flexion LDR	20.7 (5.3)	18. 8 (8.5)	19.7 (4.1)	21.3 (6.6)
†Max Knee Flexion	61.3 (6.1)	61.7 (8.4)	58.4 (5.6)	60.3 (6.4)
*Pain	0.0 (0.0)	0.0 (0.0)	0.0 (0.2)	0.5 (0.7)
*Overall QoL	100.0 (0.0)	100.0 (5.28)	97.3 (10.1)	94.6 (17.4)

†Values are in mean (SD), \*values are median (IQR).

### 7.5.7 Relationship between Knee JK and JPS in Healthy Children

The relationship between knee JK and JPS in healthy children was investigated using correlation analyses. JK data was not normally distributed (Shapiro-Wilk test;  $p < 0.05$ ) therefore, a non-parametric correlation (Spearman correlation) was chosen. Table 7.9 presents the correlation between the different proprioception tests. Correlation analyses revealed a low and statistically non-significant correlation between JK and JPS at  $25^0$  and between the JPS tests at both  $25^0$  and  $10^0$ . Additionally, there was a low but significant correlation between JK and JPS at  $10^0$ . These findings suggest that weak correlations exist between the three different measures of proprioception.

**Table 7.9: Spearman's correlations between proprioception outcome measures (n = 37)**

Variable	r Values	p Values
JK and JPS at $25^0$	0.150	0.374
JK and JPS at $10^0$	0.385	<b>0.019*</b>
JPS at $25^0$ and $10^0$	-0.116	0.495

r = Spearman correlation coefficient: \*statistically significant at  $\alpha < 0.05$ .

### 7.5.8 Results of Healthy and HMS Children Cohorts based on Age and Gender

In the previous section, significant differences were demonstrated in the level of neuromuscular performance, functional ROM during walking and QoL between healthy children and children with HMS. Gender differences were also found in passive knee ROM and QoL (physical functioning domain) in healthy children (Table 7.9). Therefore, the results of the current study were further broken down to reflect the possible gender-specific pattern in passive ROM and physical functioning domain of QoL between the two groups. Due to gender imbalance and a small number of boys with HMS in this study, the influence of gender on the outcomes could not be investigated using inferential statistical analysis. However, descriptive statistics were carried out to show the possible influence of gender on these outcomes (passive ROM and physical functioning domain of QoL) in HMS children.

The summary of the descriptive analysis in healthy controls and HMS group based on gender are presented in Table 7.10.

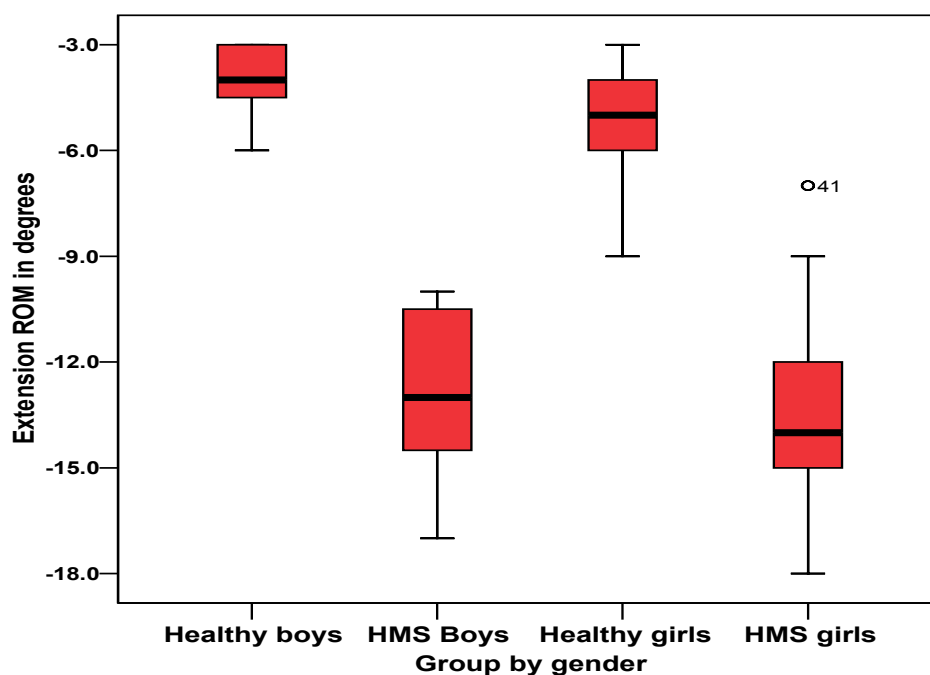


**Table 7.10: Summary of results of healthy children and children with HMS (based on age and gender).**

<b>Variables</b>	<b>Healthy Boys (n = 20)</b>	<b>Boys with HMS (n =8)</b>	<b>Healthy Girls (n = 17)</b>	<b>Girls with HMS (n = 21)</b>
ROM <sup>(0)</sup>				
*Extension	-4.0 (1.75)	-13.0 (4.5)	-5.0 (2.0)	-14.0 (3.0)
*Flexion	142.5 (6.0)	156.0 (4.3)	143.0 (5.5)	155.0 (6.5)
*QoL -Physical Functioning	100.0 (0.0)	78.1 (25.8)	100.0 (7.8)	75.0 (29.6)

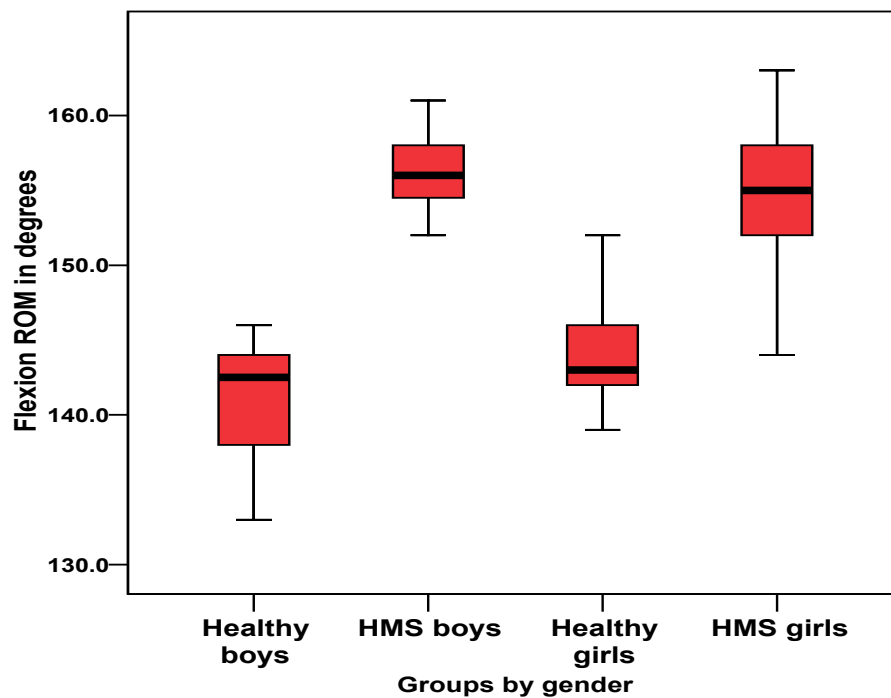
\*Values are median (IQR).

Figures 7.14 – 7.16 illustrate the median and IQR or mean and SD values of all the measurement parameters in the HMS cohort. The healthy controls are shown for comparison. From these box plots, the red boxes represent the IQR with the black line representing the median values.



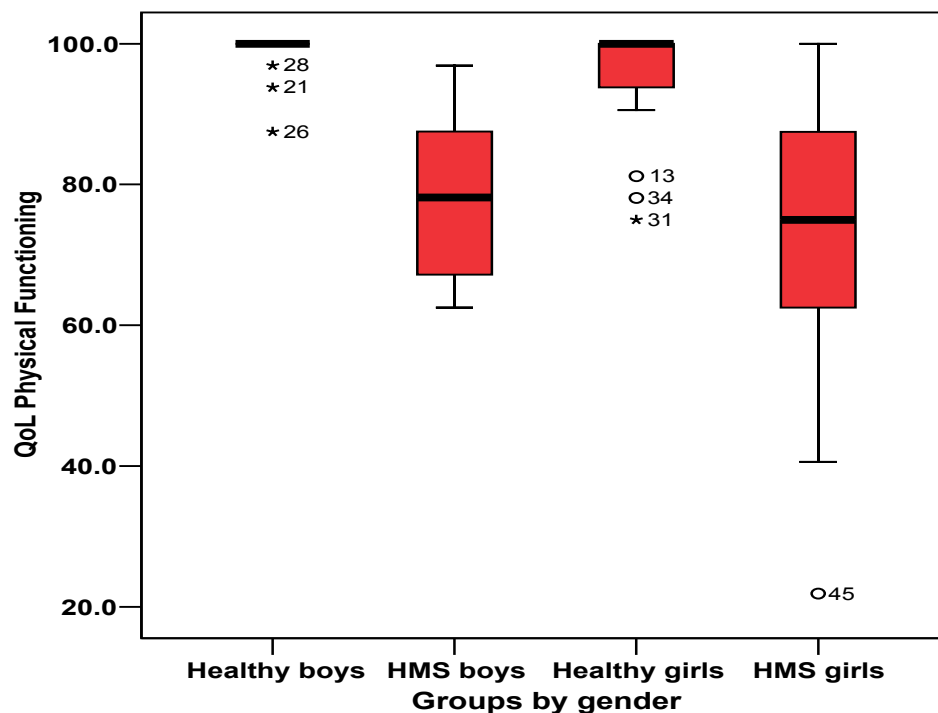
**Figure 7.14: Box plots of extension ROM in healthy children (n = 37) and children with HMS (n = 29) based on gender**

The box plots in Figures 7.14 and 7.14 illustrate the passive knee extension and flexion ROM respectively. It can be seen from the figures that the median values of both extension ROM was higher in girls with HMS than boys with HMS. Additionally, the data of knee extension ROM was widely distributed in girls with HMS than boys with HMS. However, a slightly higher median values and lesser variations of flexion ROM were found in boys with HMS than girls with this condition.



**Figure 7.15: Box plots of flexion ROM in healthy children (n = 37) and children with HMS (n = 29) based on gender**

These findings indicate that in the HMS cohort, girls had higher knee extension than boys and knee flexion was greater in boys than girls.



**Figure 7.16: Box plots of physical functioning domains of QoL in healthy children (n = 37) and children with HMS (n = 29) based on gender.**

From Figure 7.16, boys with HMS demonstrated higher median QoL scores in physical functioning domain of QoL than girls with this condition. There were larger amount of variations in the data of this domain for the girls than boys. These results indicate that in the HMS group, girls had poorer QoL (physical functioning) perception than boys.

In summary, descriptive statistics revealed that in the HMS cohort, boys achieved higher flexion ROM and QoL (physical functioning) than girls. However, girls with HMS demonstrated higher knee extension ROM than the boys. These observations should be treated with caution as inferential statistical analysis was not carried out due to small number of boys with HMS.

The following section presents the relationship between pain, neuromuscular impairments, functional ROM during walking and QoL in children with HMS.

### 7.5.9 Relationship between Beighton Scores and the Outcomes in the Present Work

Beighton scores were identified in the literature as the most frequently used method of assessing GJL in children with HMS. The relationships between Beighton scores and the measurement parameters included in the present work were examined using Pearson correlations (for parametric data) and Spearman rho correlations (for non-parametric data). The summary of the correlation analyses are presented in Table 7.11.

**Table 7.11: Correlations between Beighton scores and outcome measures in children with HMS (n =29)**

Variable	r Values	p Values
BS and Pain	-0.096	0.621*
BS and JK	-0.090	0.641*
BS and JPS at 25 <sup>0</sup>	-0.301	0.112*
BS and JPS at 10 <sup>0</sup>	0.058	0.665†
BS and Extensor Muscle Torque	-0.225	0.242*
BS and Flexor Muscle Torque	-0.152	0.431*
BS and Extension ROM	-0.315	0.096†
BS and Flexion ROM	0.076	0.696*
BS and KEMS	-0.102	0.599†
BS and KFLR	-0.014	0.468†
BS and MKF	-0.168	0.384†
BS and QoL	-0.026	0.895*

BS = Beighton Score, KEMS = Knee Extension in Mid-Stance, KFLR = Knee Flexion Loading Response, MKF = Maximum Knee Flexion. † = Pearson correlation coefficient, \* = Spearman correlation coefficient.

No correlation was found between Beighton scores and any of the outcomes (r range = -0.225 to 0.337; all  $p > 0.05$ ) in children with HMS. The largest correlation coefficient was observed between Beighton scores and flexion ROM ( $r = -0.315$ ;  $p = 0.096$ ) while the smallest coefficient was found between these scores and extension ROM ( $r = -0.014$ ;  $p = 0.468$ ). These results suggest a weak relationship between Beighton scores and any the variables measured in the present study. These findings imply that no statistically significant relationships exist between Beighton

scores and neuromuscular impairments, functional ROM and QoL indices in children with HMS.

Some findings of assessment in children with HMS and the controls presented as conference papers are illustrated in Appendices 4.2 and 4.4 to 4.9.

## **7.6 Overall Summary of Results**

This chapter has outlined the experimental design and recruitment of healthy children and those with HMS. It has also reported the level of neuromuscular impairments, functional ability and QoL in healthy children and those with HMS. The knee joint was found to be the most symptomatic (painful) joint in these children.

Impaired knee proprioception (JK and JPS), lower muscle torque (knee extensors and flexors) and increased passive knee ROM were found in children with HMS. In addition, lower knee flexion and higher knee extension during walking were observed. Children with HMS experienced more pain and exhibited poorer QoL in comparison with the healthy controls. Correlation analyses demonstrated weak relationships between pain, neuromuscular impairments and functional ROM during walking in children with HMS. However, a strong correlation was found between pain and QoL in these children. The correlation between Beighton scores and all the variables included in the present work was weak.

No gender difference was found in all the outcomes between healthy boys and girls except for knee ROM (extension and flexion) and QoL physical functioning. Investigation of the effect of age on all the outcomes in healthy children indicated that there was no age-related difference on the variables measured except for JK, extension ROM, pain and overall QoL and its domains (except for physical functioning). Correlation analyses revealed a poor relationship between knee JK and JPS tests in healthy children.

The following chapter will discuss the results of neuromuscular impairments, activity limitations and participation restrictions in children with HMS. The level of neuromuscular performance, functional ability and participation in healthy children will also be examined. The strengths and implications of these findings in relation to assessing children with HMS are also examined.

## **CHAPTER 8 : DISCUSSION**

### **8.1 Introduction**

The results for the assessment of neuromuscular performance, functional range of motion (ROM) and quality of life (QoL) in children with hypermobility syndrome (HMS) and healthy children have been presented in chapter 7. The findings were that children with HMS had a number of neuromuscular impairments (joint kinaesthesia (JK), joint position sense (JPS), reduced knee extensor and flexor muscle torque and increased pain perception), reduced knee flexion and increased knee extension in gait, and poorer QoL when compared to healthy children. To clearly address the aims (primary and secondary) of the current programme of work (see section 1.3), these findings will be discussed in this chapter under the following sub-headings:

1. Comparisons of neuromuscular performance, functional ROM and QoL characteristics between healthy children and those with HMS.
2. The relationships between pain and each of the following: other neuromuscular impairments (joint proprioception, muscle torque and passive ROM), functional ROM during level walking and QoL.
3. The relationships between Beighton scores and all the features found in association with HMS in children.
4. Neuromuscular performance, functional ROM during walking and QoL characteristics in healthy non-symptomatic children.
5. Gender- and age-related differences in neuromuscular performance, functional ROM and QoL characteristics in healthy children.
6. The relationship between JK and JPS tests in healthy children.

## **8.2 Comparisons of Neuromuscular, Functional ROM and QoL Characteristics between Healthy Children and Children with HMS**

The primary focus of this thesis was to identify the possible level of impairments, activity limitations and participation restrictions in children diagnosed with HMS. Data on these indices were therefore collected in healthy children and those with HMS to identify any deviation from normality in children with HMS. Comparisons of data between healthy children and HMS cohorts revealed significant differences in all the outcomes (all  $p < 0.001$ ) except for walking speed.

Studies of neuromuscular impairments in children have been limited to pain (Hakim and Grahame 2004; Adib et al. 2005), muscle torque (Engelbert et al. 2003; 2004; 2006) and motor development (Jaffe et al. 1988; Engelbert et al. 2005). Only epidemiological studies of pain in children with HMS have been reported (Biro et al. 1983; El-Garf et al. 1998; Qvindesland and Jonsson 1999; Vougiouka et al. 2000). Apart from Sacheti et al. (1997) who reported pain intensity in children and adults with HMS, however, to date, pain intensity has not been well reported in children with this condition. The author of this thesis is also not aware of any studies that have investigated joint proprioception (JK and JPS), functional ROM or QoL in children with HMS. Therefore, the present investigation presents original findings on these variables. Due to lack of available published data on these symptoms in children with HMS, the findings of the present study are examined in relation to the existing literature in adults. Please note that the term 'muscle torque' is again used in place of muscle strength in this chapter. This section discusses the level of neuromuscular impairments, activity limitations and participation restrictions identified in children with HMS.

### **8.2.1 Pain**

Pain is the most common neuromuscular complaint that has been assessed in children with HMS (Biro et al. 1983; El-Garf et al. 1998; Qvindesland and Jonsson 1999; Vougiouka et al. 2000). Joint pain in adults with HMS has also been reported (Ferrell et al. 2004). The mean pain intensity of 51 patients (age range = 9 - 70 years) with HMS and associated Ehlers-Danlos syndrome (EDS) was reported by Sacheti et al. (1997). In that study, pain intensity was found to be 5.3 on the McGill Pain Questionnaire (scale, 0-10). It is difficult to compare pain intensity reported by Sacheti et al. (1997) with that observed in the present study for two reasons. First,

they examined pain intensity using the McGill Pain Questionnaire while a coloured analogue scale was used in the current study. Secondly, subjects were made up of children and adults with HMS and associated EDS, a condition that is believed to predispose to musculoskeletal pain (El-Garf et al. 1998). In relation to patients with HMS, Sacheti et al. (1998) was the first to report pain intensity in patients with this condition (HMS). The present study examined pain intensity in children with HMS.

The result of the current study on pain contrasts with the findings of Mikkelsen et al. (1996) who observed that children with generalised joint laxity (GJL) did not experience more pain than healthy controls (those without GJL). An unspecified questionnaire was used to assess pain in the study of Mikkelsen et al. (1996) while pain was evaluated with a coloured analogue scale (CAS) (previously validated by McGrath et al. 1996) in the present study. Furthermore they examined children with GJL and not those with HMS. As a result, their observation may not be applicable to children with HMS.

The finding of the present study supports the notion that children with HMS experience knee pain more than their healthy counterparts (Everman and Robin 1998; Cherpel and Marks 1999). The cause of knee joint pain in children with HMS is not known, although in some of the children with HMS in the present study it was reported to be activity-related. Hence, their pain could have been due to repetitive micro-trauma or wear and tear on the knee joint surface (Simpson 2006) resulting from physical activity (Everman and Robin 1998). In addition, knee joint instability resulting from ligamentous laxity (Maillard and Murray 2003) due to impaired collagen fibres (Bird 2005) may also lead to soft-tissue micro-trauma (Gedalia and Brewer 1993) in children with HMS. Impaired knee joint proprioception has been reported in patients with HMS (Hall et al. 1995) suggesting that sensory feedback from the affected joints of these patients may be diminished. This impairment may lead to biomechanically unsound limb positions being adopted by these children and may cause repetitive micro-trauma of their knee joint. Knee pain may also occur for other reasons, such as enhanced tissue sensitivity or recent sprains/strains of the soft tissues surrounding the joint (Adib et al. 2005; Simpson 2006). However, knee joint in the present study is unlikely to be due to sprains/strains as they were part of the exclusion criteria used in the present research.



In the present study pain intensity in children with HMS may not be accurate for the following reasons: 1) only a certain proportion of the children had pain during the assessment; 2) average pain was measured as a result it is possible that children might not remembered what their pain level was in the past week; 3) some of the children with HMS were undergoing treatment for pain during the time of testing. The present study is the first to report pain intensity in children with HMS and therefore the results can be used as a reference with which pain scores in future studies of HMS in children could be compared.

The implication of this finding is that pain intensity assessment should be considered when assessing children with HMS and they may benefit from therapeutic intervention directed towards alleviating their pain. In addition, establishing pain intensity in these children will help clinicians to evaluate the effectiveness of pain management in HMS. It has been proposed that hydrotherapy, counselling (the child and the parent), hot and cold packs, transcutaneous electrical nerve stimulation (TENS), massage, and relaxation and distraction techniques may be beneficial in relieving pain in children with this condition (Maillard and Murray 2003). The present researcher is unaware of any study that has reported the effectiveness of any of these treatment methods for pain management in children with HMS. Therefore future studies may be directed towards developing a strategy for alleviating pain in children with this condition.

### **8.2.2 Proprioception**

The present investigation is the first to examine knee joint proprioception in children with HMS. Since GJL is one of the features seen in HMS (Engelbert et al. 2003; 2004; 2006) and impaired knee joint proprioception has been found in association with GJL (Barrack et al. 1983a; Rozzi et al. 1999), the observations in the current study were compared with findings in adults with GJL as well as those with HMS.

Within the present study, knee proprioception (JK and JPS) values were observed to be significantly higher (both  $p < 0.001$ ) in children with HMS compared with their healthy counterparts (i.e. children with HMS had diminished proprioceptive acuity). Impaired joint proprioception in women with HMS was first reported by Mallik et al. (1994). The knee joint, which is believed to be the joint most affected by the symptoms of HMS (Kerr et al. 2000; Vougiouka et al. 2000; Adib et al. 2005), was

not examined by Mallik et al. (1994). Therefore, their findings may not be directly applicable to the knee joint of children with HMS.

The result of JK in this investigation agrees with the observation of Hall et al. (1995) who observed impaired knee JK in adults with HMS. These authors found that knee JK was significantly worse ( $p < 0.0001$ ) in 10 women with HMS (mean age 30 years) than their age-matched healthy controls. Hall et al. tested knee JK with cutaneous sensation eliminated by means of an air splint. Due to the reasons earlier stated (section 5.2) an air splint was not used in the present study but JK was also found to be significantly worse in children with HMS compared with the controls. The study of Hall et al. has the advantage of being the first study to examine knee JK (the joint most affected by symptoms of HMS) in patients with HMS. However, the sample size in their study was small and only JK, one component of joint proprioception, was tested. Consequently, the results of Hall et al. (1995) cannot be generalised, as their sample may not be representative of patients with HMS. In addition, their findings on JK may not represent the overall proprioceptive ability as only one aspect was examined.

Impaired knee joint proprioception has also been reported in GJL (Barrack et al. 1983a; Rozzi et al. 1999) and ACL deficient knees (Corrigan et al. 1992; MacDonald et al. 1996; Borsa et al. 1997; Beynnon et al. 1999; Roberts et al. 2004). Although the above researchers demonstrated that knee joint proprioception was significantly poorer in individuals with joint laxity compared with healthy controls, differences in the participants' characteristics and methods of testing limits the comparison between these studies and the current investigation.

On the other hand, the present findings on JPS contrast with the results of active JPS reported by Stillman et al. (2002). They tested active knee JPS in 44 healthy subjects who had a history of regular sports spanning more than 5 years. These participants were classified into more mobile and less mobile groups based on their passive knee extension measurement using a video-based technique. They found that JPS error was statistically better in subjects with greater knee joint mobility than those with less mobility. Muscle receptors are believed to play an important role in joint proprioception (Skinner et al. 1986; Grigg 1994; Lattanzio et al. 1997). Proprioceptive contribution from muscles acting on the knee joint during active JPS

testing could therefore have influenced the findings of Stillman et al.. It is believed that joint proprioception may be enhanced by exercise training (Petrella et al. 1997; Ashton-Miller et al. 2001; Roberts et al. 2004). Stillman et al. did not state if participants with greater knee mobility engaged in sports more than those with less knee mobility. Therefore, it is unknown whether the level of physical activity participation of the subjects with greater knee mobility played a role in the lower JPS error recorded in those subjects as their knee JPS could have been improved by exercise.

Active knee JPS testing, as performed by Stillman et al. (2002), has been reported to be more repeatable and accurate than passive JPS testing (Stillman et al. 2002), as used in the current study. Additionally, active JPS may reflect individuals' functional status better than passive JPS tests as it involves both sensory skills and motor contribution from the muscles acting on the examined joint (Tsang and Hui-Chan, 2003). Active JPS tests may not be appropriate in individuals with knee pain or pathological conditions where voluntary contractions of muscles acting on the examined joint are impaired. When testing these individuals, a passive JPS test may be required to minimise motor contribution to proprioception. Considering the characteristics of the participants in the present study, the passive JPS test was employed.

The higher values of JK and JPS errors observed in children with HMS in the current study indicate impaired knee joint proprioception. The reasons for proprioception deficit in the current study are not known. Proprioception can be influenced by the progestogen dominated phase of the menstrual cycle (Aydog et al. 2005; Friden et al. 2006). For example, knee JPS deficits were observed in the menstrual phase (Aydog et al. 2005) and impaired knee JK was detected during the premenstrual phase (Friden et al. 2006) of the menstrual cycle in healthy women. In the present study, information regarding menstruation and age of menarche was not collated and as a result the researcher was unable to determine when measurements were taken in relation to the menstrual cycle. Group comparisons of JK and JPS data based on gender revealed that girls with HMS had significantly poorer ( $p < 0.05$ ) knee joint proprioception compared with their healthy counterparts. Therefore, the author of this thesis cannot say for sure whether menstrual cycle had any effect on the findings on knee proprioceptive acuity in children with HMS or not.

Diminished muscle spindle activation has been proposed to be responsible for proprioception deficit (Hurley et al. 1997). Muscle spindle sensitivity is controlled by the  $\gamma$ -motoneurone system and diminished activation of this system causes decreased muscle spindle sensitivity, resulting in proprioception impairment (Hurley et al. 1997). In the present study, passive JPS was administered, as this is thought to maximally stimulate joint mechanoreceptors while minimally stimulating muscle receptors (Barrack et al. 1989). To reduce proprioceptive input from the muscles acting on the examined joint during knee joint proprioception testing, an EMG was used by Beynnon et al. (1999) to monitor the activities of the muscles. Due to the reasons stated in section 5.2 of this thesis, EMG was not used in the present study. However, the test limb was placed in a padded limb support during proprioception testing, ensuring that the muscles acting on the test limb were relaxed as it is believed that muscular mechanoreceptors function mainly to signal active muscle tension during muscle contraction (Jami 1992; Wilson et al. 1999). It can, therefore, be assumed that proprioceptive contribution from muscle spindles and/or Golgi tendon organs located in the muscles acting on the knee joint was reduced during proprioception testing (in both healthy children and those with HMS). Hence, it is unlikely that the impaired knee joint proprioception observed in the present study was due to diminished muscle spindle sensitivity in children with HMS.

Impaired joint proprioception in children with HMS may be due to diminished proprioceptive discharge from the joint receptors (Mallik et al. 1994). The mechanisms responsible for the impaired proprioceptive discharge in individuals with HMS are not understood. Hyperextension of the knee joint is prevented by the posterior portion of the joint capsule, and the posterior cruciate and collateral ligaments (Moore and Dalley 1999). Joint hyperextension is thought to be related to laxity of these structures (Hall et al. 1995). In the current study, passive knee extension was found to be statistically higher (Table 7.3) in children with HMS than the controls, indicating that they exhibited some degree of knee hyperextension. Therefore, the diminished proprioceptive discharge from articular mechanoreceptors may be related to damage to these mechanoreceptors or defect in the articular tissues resulting from excessive joint mobility and abnormal biomechanics of their knee joint (Mallik et al. 1994).

Moreover, impaired knee joint proprioception may be due to diminished joint proprioceptor activation caused by capsular or ligamentous stretching in the lax joint (Mallik et al. 1994). This may cause children with HMS being unaware of placing abnormal stress on their joints by moving them into positions outside their normal ROM (Mallik et al. 1994). It has also been suggested that repetitive stresses on joints may lead to ligamentous laxity causing damage to the joint receptors and further impairing proprioception at these joints (Mallik et al. 1994). Any or all of these hypotheses may be the case in children with HMS in this investigation. The likely mechanisms for proprioceptive deficit in individuals with HMS and GJL have been summarised in Figure 2.3 of this thesis.

The current findings on JK and JPS acuity suggest that knee joint proprioception may be impaired in children with HMS. It has been suggested that disturbed knee proprioception can lead to biomechanically unsound limbs (Ludon 2000) and altered joint stability and control of joint motion (Barrack et al. 1983a). Impaired knee joint proprioception can also cause a deficit in motor control and functional performance (Marks 1997) such as walking (Barrett et al. 1991). The findings of the present investigation could imply that a loss of proprioceptive acuity may affect normal functional performance in children with HMS. Therefore, knee joint proprioception assessment should be included as part of clinical examination of children with this condition. Supportive splints (Birmingham et al. 2001; Herrington et al. 2005), elastic bandage (Barrett et al. 1991), joint taping (Perlau et al. 1995) and exercise training (Ferrell et al. 2004; Sekir and Gür 2005) have been shown to improve knee joint proprioception. Hence, appropriate intervention programmes aimed at improving joint proprioception should be developed by clinicians for children with HMS.

### **8.2.3 Muscle Torque**

In the current investigation, knee muscle torque (of the extensors and flexors) was observed to be significantly lower (both  $p < 0.001$ ) in the HMS cohort than their healthy counterparts. These findings agree with those of Sahin et al. (2007) who observed a significant deficit in knee extensor muscle torque in adults with HMS compared with healthy controls. On the other hand, Engelbert et al. (2003) found a higher but non-significant value of 'total muscle torque' (N) in 79 healthy children compared with 15 children with HMS. Engelbert et al. (2004) also reported higher values (but not statistically significant) of 'total muscle torque' in healthy children

than those with HMS. Total muscle torque was calculated as the summation of measurements of shoulder abductors, grip strength, and hip flexors.

In these two studies (Engelbert et al. 2003; 2004), 'total muscle torque' of shoulder abductors, hip flexors, ankle dorsiflexors and grip strength was examined using a hand-held myometer. Moreover, Engelbert et al. (2003) reported muscle torque whereby the moment arm of joints measured was not taken into consideration. Muscle torque has been reported to be a function of the moment arm (Smidt and Rogers 1982; Keating and Matyas 1996) as the force applied to the myometer's transducer may vary with the distance from the axis of the examined joint. Therefore, the farther from the joint axis the transducer is placed, the less the force registered by the transducer during maximum contraction (Keating and Matyas 1996). The moment arm is defined as the product of muscle force and the perpendicular distance from the joint axis to the transducer (Keating and Matyas 1996). This is an important consideration when comparing the results of Engelbert et al. (2003) to the present study.

A reduced (but not statistically significant,  $p > 0.05$ ) muscle torque was observed in children with HMS compared with the controls by Engelbert et al. (2006), when 'total muscle torque' (in Newtons) of shoulder abductors, hip flexors and grip strength in 13 children with HMS was examined using a hand-held myometer. In that study, 8 physiotherapists carried out muscle torque measurements in which both the intra- and inter-tester repeatability was acknowledged to be high. However, no reference was made to other factors that could influence muscle torque measurement such as verbal encouragement. It is therefore not clear whether this was consistent in their study or not. It has been shown that verbal encouragement significantly increased muscle torque (McNair et al. 1996). In addition, muscle torque measurement was performed three consecutive times by Engelbert et al. (2006) and highest value was recorded whereas measurement was carried out once in the present study. Therefore the lack of significant difference observed by Engelbert et al. (2006) may be due to these factors.

On the other hand, Engelbert et al. (2004) did consider the moment arm in their study and reported muscle torque in Newton meters. However, their values were not normalised to body mass, which has been reported to influence myometer measurements, with heavier subjects tending to produce higher values than lighter subjects (Hald and Bottjen 1987). In addition, Engelbert et al. (2003; 2004) examined 'total muscle torque' of upper and lower limbs, while knee muscle torque was examined in the present study. Although not all the participants in the present study presented with painful knee joints at the time of assessment, the joints examined by Engelbert et al. (2003; 2004) are not the most commonly affected by the symptoms of HMS and it is possible that these joints were not symptomatic. The sample sizes of the HMS groups used in these previous studies were small (n range = 13 – 19 participants), limiting the generalisability of their findings.

The studies by Engelbert et al. (2003; 2004; 2006) were the first and only investigations found that have quantified muscle performance in children with HMS. The present study has some advantages in comparison with those investigations. First, using a fixed digital myometer for assessing knee joint torque in the current study ensured that each subject's extremity was properly stabilised. The hand-held myometer used by Engelbert et al. (2003; 2004; 2006), may be difficult to stabilise against the subject's extremity, thus predisposing it to measurement error. Bohannon and Andrews (1987) observed that stabilisation of the subject's extremity was essential for obtaining repeatable measurements using a hand-held myometer. The between-days repeatability of the digital myometer used in the present study was found to be excellent (ICC range = 0.85 to 0.98) whereas in the studies by Engelbert et al. (2003; 2004; 2006) this was not reported. Although this does not negate the ability of their method to detect group difference it limits the generalisability of their findings. The strengths of the current investigation provide evidence in support of the validity of its findings.

The reasons for the reduced muscle torque in children with HMS are not known. Laforrest et al. (1990) demonstrated that knee flexion and extension muscle torque for both young and old tennis players were greater than the values obtained for sedentary subjects who were matched for age, height and lean body mass, indicating that training has a significant role in muscle torque. Adib et al. (2005) also found that the majority of the children with HMS did not engage in routine exercise,

such as physical education at school. In addition, Engelbert et al. (2006) observed that participation in sports activities was significantly ( $p < 0.05$ ) less in children with HMS than the controls. Therefore, it was thought that the level of physical activity in children with HMS could have been responsible for the current findings on muscle torque. However, this was unlikely in the present study because independent t-test analysis revealed no significant difference ( $p = 0.740$ ) in the level of physical activity between healthy children and those with HMS.

The lower values of muscle torque recorded by the HMS group may be due to incomplete voluntary activation of muscles acting on the painful knee joint (Hurley and Newman 1993; Hurley et al. 1994; Hurley et al. 1997). In the present study some of the children with HMS complained of knee pain during muscle torque measurements. This may have impaired maximum muscle contraction. This was a subjective observation that requires further investigation in children with this condition. Nonetheless, this study has provided evidence that knee muscle torque deficit may be found in children with HMS and implies that muscle torque assessment should be incorporated into clinical examination of children with HMS. Knee muscle strength has been shown to be a determinant of lower limb functional activities (Bearne et al. 2002; Liu-Ambrose et al. 2003) and impaired muscle function may not only result in muscle weakness but also cause a deficit in proprioceptive acuity (Hurley et al. 1998). In addition, it is believed that good quadriceps muscle performance is important for activities of daily living (ADL) such as standing up, sitting down, climbing and walking. Decreased quadriceps torque may therefore be associated with impaired functional activities (Stucki et al. 1998) and ADL performance (Hurley et al. 1998).

Given the present findings on knee muscle torque, it may be worth assessing muscle performance during clinical examination of children with HMS. The findings also suggest that muscle strengthening programmes may be beneficial to children with HMS. The author of this thesis is not aware of any published data on muscle torque improvement in children with HMS however exercise programmes have been found to enhance muscle torque in healthy children and children with pathological conditions. Increased hamstring and quadriceps muscle torque has been found in healthy children (Ramsay 1990; Faigenbaum et al. 1993), children with cerebral palsy (Morton et al. 2005) and adults with HMS (Ferrell et al. 2004) following



strength training. Improved knee extensor muscle torque has also been demonstrated in children with burn injuries (Suman et al. 2001) and adults with rheumatoid arthritis (Bearne et al. 2002) after exercise programmes. Based on these observations on muscle torque in healthy children and those with pathological conditions, it would appear that muscle torque may be improved in children with HMS using strength training. Therefore, clinicians are to be aware of muscle torque deficits in children with HMS and should develop appropriate muscle strengthening programmes.

#### **8.2.4 Range of Motion (ROM)**

Passive knee extension and flexion ROM were significantly higher (both  $p < 0.001$ ) in children with HMS than the controls. Apart from the study by Engelbert et al. (2004), no study was found reporting knee ROM in children with HMS. Engelbert et al. (2004) investigated active knee flexion and extension in 19 children (aged  $11.6 \pm 2.7$  years) with HMS and 274 healthy controls (aged  $12.8 \pm 3.3$  years). They found that children with HMS had significantly reduced knee flexion ROM and higher knee extension ROM compared with healthy controls. The findings of Engelbert et al. (2004) could not be compared directly with the results of the present study due to methodological differences, as passive ROM was measured in the present study whereas Engelbert et al. (2004) examined active ROM.

Active ROM examined by Engelbert et al. (2004) is more functional and clinically relevant than passive ROM as functional tasks are carried out using active movement. Passive ROM, however, as measured in the present study, has two advantages over active ROM. It could help to overcome limitation of knee ROM that may be due to pain (Norkin and White 2003). Passive ROM may also be more useful to determine the overall joint mobility in children who may be unwilling to perform active ROM (Norkin and White 2003).

Engelbert et al. (2003) found that 'total passive ROM' (consisting of shoulder, elbow, wrist, hip, knee and ankle joints) was significantly higher in children with HMS (mean age  $\pm$  SD =  $8.1 \pm 0.6$  years) than healthy children (mean age  $\pm$  SD =  $9.2 \pm 0.1$ ). However, the present findings cannot be directly compared with that of Engelbert et al. (2003) because only passive ROM of the knee joint was measured in the present study. Since the knee is most frequently affected by the symptoms of HMS, the

findings of the present study provide original data with which future studies on knee ROM in children with HMS can be compared.

It has been reported that healthy girls exhibit a greater ROM than boys (Jasson et al. 2004; Seckin et al. 2005; Bird 2007). The increased passive knee ROM observed in children with HMS could therefore be attributed to gender imbalance in the subjects recruited for the present study, as significant differences were observed (both  $p < 0.05$ ) in passive knee extension and flexion ROM between healthy boys and girls (Table 7.6). However, this was unlikely because Mann-Whitney U test further indicated significant difference ( $p < 0.05$ ) between healthy girls and girls with HMS. The possible explanation for the increased passive ROM in the HMS cohort is that ROM may be a function of ligamentous laxity of the knee joint that is probably inherited by these children (Grahame et al. 1999). In addition, the increased joint ROM in children with this condition may be the result of the observed muscle torque deficit (Table 7.3), as the amount of joint ROM is determined by the strength and flexibility of the surrounding soft tissues, including muscles (Everman and Robin 1998).

The present study suggests that ligamentous laxity may also play a role in increased knee ROM. Given the results of the current study and the functions of both the anterior and posterior cruciate ligaments (Moore and Dalley 1999), it would appear that both ligaments might also be responsible for the increased knee ROM observed in children with HMS. Further investigations are required to determine the exact ligaments of the knee that are affected by ligamentous laxity in children diagnosed with HMS.

The present finding on knee extension ROM suggests that knee hyperextension seen in children with HMS may be partly due to ligamentous laxity (Hall et al. 1995) of the knee joint. Since knee ROM was significantly higher in children with HMS in this study, an objective quantification of joint ROM may be required as part of clinical examination of children with HMS. Solomonow et al. (1987) suggested that knee joint laxity decreases substantially when the stabilising muscles have higher baseline tone at rest. Knee joint stability is believed to be maintained by increased hamstring muscles activity (Barrata et al. 1988). These muscles pull back the anteriorly displaced tibia reducing knee joint laxity as the loading conditions change

during physical activity. Reduced knee ROM was reported in patients with HMS following a six week exercise programme (Barton and Bird 1996). Combining these theories (Solomonow et al. 1987; Barrata et al. 1988) and the findings of Barton and Bird (1996), it seems that stability-type exercise may help to reduce excessive joint ROM in children with HMS. Therefore, to improve the stability and protect the integrity of symptomatic joints in children with this condition, physiotherapy treatment intervention that includes stability-type exercise should be considered.

### **8.2.5 Functional ROM**

Knee extension during walking was significantly higher ( $p < 0.001$ ) in children with HMS than the controls. Additionally, knee flexion (during loading response and maximum flexion in swing phase) during walking was significantly ( $p < 0.001$ ) lower in children with HMS than the controls. To date, functional ROM during walking has not been investigated in either children or adults with HMS. Hence, the findings of the current study on functional ROM could not be compared with any previous study. The reasons for the reduced knee flexion and increased knee extension during walking are unclear. Based on ICC and 95% limits of agreement, some of the functional ROM parameters were found to have low between-days repeatability in healthy children and those with HMS (Tables 6.2 and 6.3). However, t-tests demonstrated no significant differences ( $p$  range = 0.328 to 0.875) between repeated measurements (one week apart) of functional ROM parameters. In addition, it has been demonstrated that knee flexion angle at the end of loading/midstance increases with higher walking speed (Stansfield 2001), and diminished knee flexion during walking has been attributed to reduced walking speed (van der Linden et al. 2002). The process of measuring the walking speed was not described in the method section as this was not one of the primary or secondary aims of the study. However, since this was also recorded by the VICON camera system during walking the researcher felt that the possible effect of walking speed on functional ROM should be examined. Within the present study, there was no significant difference ( $p = 0.496$ ) in walking speed between the controls and HMS group.

A possible reason for these results of functional ROM may be that, on account of joint laxity, children with HMS could have increased knee varus/valgus compared with controls due to laxity of the knee joint. Increased varus/valgus movement may prevent normal sagittal motion of the knee joint during walking. This is just an

assumption, as varus/valgus motion was not calculated in the present study. However, it may serve as an area for future investigation. It has also been suggested that reduced knee flexion during walking may be due to muscle weakness (Perry 1992). Therefore, the increased knee extension and reduced knee flexion during walking may be the result of diminished knee muscle torque that was observed in children with HMS in the present study (Table 7.3). An alternative hypothesis for the current findings on functional ROM may be the result of impaired knee JPS, as it has been suggested that this causes people with HMS to move their joints to positions outside their normal ROM (Mallik et al. 1994). This could also have been the case in this study as children with HMS (Table 7.3) demonstrated significantly higher JPS errors at both target angles.

The present investigation is the first to report functional ROM during walking in children with HMS, making it one of the strengths of this thesis. In addition, this study has provided reference values of knee kinematics data in these children with which future investigations can be compared. The current findings on functional ROM imply that children with HMS walked with a knee hyperextension gait pattern. Gait kinematics assessment in children diagnosed with HMS may be useful and they may benefit from programmes of gait re-education.

#### **8.2.6 Quality of Life (QoL)**

Poorer overall QoL (and each of its domains) were found in children with HMS compared to the controls (Table 7.3). Again, the researcher is not aware of any previous study on QoL in children with HMS. However, one study was found by the researcher investigating physical and psychosocial well-being of healthy school children with GJL (Ruperto et al. 2004). Since HMS is considered to be a rheumatological condition, the present findings on QoL are also discussed in relation to studies in children with rheumatological conditions (Varni et al. 2001) and adults with HMS (Ferrell et al. 2004).

In Ruperto et al.'s study, it was found that both physical and psychosocial well-being were not limited in children with GJL compared with controls. Children with GJL were, however, found with more social limitation compared with controls. Due to the reasons already discussed in section 2.4 of this thesis, it is difficult to make detailed comparisons of the findings of Ruperto et al. with those of the present study on QoL as their findings may not be applicable to those with HMS.

The present findings agree with the observation of Varni et al. (2001) who found that children with rheumatic diseases had significantly poorer QoL than their healthy counterparts. Similarly, Gutiérrez-Suárez et al. (2007) found that children with Juvenile Idiopathic Arthritis (JIA) had poorer QoL compared with their healthy peers, particularly in the physical functioning domain. Ferrell et al. (2004) investigated QoL in adults with HMS and observed that Global SF-36 scores improved significantly in 18 patients (mean age  $27.3 \pm 10.4$  years) following an exercise intervention. The study of Ferrell et al. (2004) has the advantage of being the first to report QoL in patients with HMS. There was no parallel control group however, and therefore no conclusion can be drawn regarding the level of QoL in their patients relative to a healthy population. In addition, a small sample of adults was examined in their study, meaning that their findings may not be directly applicable to children with HMS. The present study adds to the database on QoL of HMS in children.

A high prevalence of anxiety disorders has been found in adults rheumatological patients with GJL (Bulbena et al. 1993). In addition, Martin-Santos et al. (1998) also observed an association between GJL and panic disorder in patients diagnosed with anxiety disorders (panic disorder and or agoraphobia). A significant correlation between GJL and anxiety disorders was found in adults receiving medical check-up (Bulbena et al. 2004).

In the present study, children with HMS were found with poorer QoL in each domain than the controls suggesting that poorer level of QoL may be associated with HMS in children. The findings of the current study could not be examined in relation to these previous studies due to differences in the participants' characteristics.

Several hypotheses may explain the present findings of QoL. It has been suggested that anxiety in individuals with HMS may be due to pain and joint instability resulting from joint laxity (Russek 2000). Hence, poorer QoL found in children with this condition in the present study could be the result of these factors. The impaired QoL in physical functioning found in children with HMS may be due to pain, decreased muscle torque and impaired joint proprioception. In addition, GJL, increased ROM of the knee joint and abnormal gait patterns observed in children with this condition could have been responsible for the impaired QoL found in these children. The lower emotional and social functioning scores may also be related to pain intensity,

as some children with HMS reported anecdotally that they had to give up routine exercise, such as physical education and sporting activities because of pain. Again, this observation is mere speculation as it was not examined objectively in this study.

Examination of the QoL data revealed that the HMS group had difficulty in writing compared with the controls. These children also reported absence from school more than the healthy group, which may be the result of pain. The lower school functioning observed in children with HMS may be due to these factors. Difficulty in writing may represent poor coordination of fine and gross motor development (Adib et al. 2005) in children with HMS. It must be noted that difficulty in writing and absence from school were not formally assessed in children with HMS in this study. Therefore, these observations also warrant further clarifications.

The current concepts of symptoms of HMS in children are mostly based on neuromuscular impairments such as pain (Adib et al. 2005), muscle torque (Engelbert et al. 2003; 2004; 2006) and motor development (Engelbert et al. 2005) while QoL aspects have not been investigated. The observations in this study, suggest that children with this condition have poorer QoL perception than their healthy counterparts and therefore provide justification for its assessment in these children.

It is believed that if a child with HMS has an understanding of the condition and is reassured that it is important to maintain as normal a life-style as possible (Middleditch 2003) he or she can cope well with the psychological issues (a component of QoL) associated with HMS. Therefore, the author of this thesis hopes that the results of the present study will help clinicians to improve the level of QoL in children with HMS by providing appropriate treatment. Such treatment, as suggested by Murray and Woo (2001), may include psychological support and counselling. In addition, since physical activity (Murray and Woo 2001) and school absence (Adib et al. 2005) may be related to pain, appropriate treatment directed towards impairments and activity limitations may also help to improve QoL in children with HMS. Management strategies in relation to this are described by Middleditch (2003). The author of this thesis did not find any study conducted on QoL treatment in children with HMS, however, the strategies proposed by Murray

and Woo (2001) and Middleditch (2003) could serve as a useful guide for managing this feature in children with HMS.

In summary, the evidence reported in this thesis has added to the current knowledge of clinicians, in particular physiotherapists, in terms of the clinical features associated with HMS in children. The thesis has demonstrated that children with HMS had neuromuscular impairments (proprioception and muscle torque deficits, increased pain and ROM). These children were also seen with activity limitations (abnormal gait patterns). Participation restrictions (poorer QoL perception) were also observed in children with HMS. It is anticipated that the findings reported in this thesis will help clinicians in the areas of assessment and management of children with this condition.

### **8.3 Age of Onset of Symptoms and Most Symptomatic Joints**

The mean age of onset of symptoms reported in boys and girls with HMS was  $6.2 \pm 3.5$  years and  $8.0 \pm 2.7$  years respectively. The finding that symptoms appeared earlier in boys than girls confirms the finding of Qvindesland and Jonsson (1999). In the present study, the overall mean age of onset of pain in children with HMS was  $7.5 \pm 3.0$  years. This is higher than that reported by Adib et al. (2005) (6.2 years) in 125 children with HMS. It is difficult to compare the findings of Adib et al. (2005) with the present study because of the different age characteristics of the participants in the two studies. The age of diagnosis of symptoms of HMS was not examined in the current investigation making it a limitation compared with the study of Adib et al. (2005) who reported that the mean age of diagnosis was 9.0 years. The age of onset observed in the current investigation is indicative of a possible delay of 1.5 years between age of onset of symptoms and diagnosis of HMS. This observation therefore, suggests that children with HMS may not receive appropriate and timely intervention for their condition which could make their symptoms difficult to treat.

Within the present study, the knees and ankles were observed to be the most frequently reported joints with adverse symptoms. These findings agree with the observations of Kerr et al. (2000) and Adib et al. (2005). Vougiouka et al. (2000) also reported that the knee was most affected by pain in children with HMS. This observation may be because, as these joints are involved in weight-bearing activities, they are prone to greater biomechanical stress than other joints (Kerr et al. 2000).

Given that the present study suggests that there may be a delay in the diagnosis of HMS in children, it would appear that early identification of the symptoms of HMS would have major implications for subsequent prevalence of some medical disorders associated with HMS (low back pain, chronic pain syndromes and degenerative osteoarthritis) that may be seen in adulthood (Lewkonja and Ansell 1983; McCormack et al. 2003; Bird 2005). In addition, this will also help both the clinicians and children with this condition in terms of developing an effective management strategy for the identified symptoms.

#### **8.4 The Relationship between Pain, Neuromuscular Impairments, Activity Limitations and Participation Restrictions in Children with HMS**

One of the aims of this thesis was to determine the relationships between pain and each of the following: other neuromuscular impairments (proprioception, muscle torque, passive ROM); activity limitation (functional ROM during walking); and participation restrictions (overall QoL and its domains) in children diagnosed with HMS. No statistically significant correlation ( $r$  range = -0.479 to 0.271;  $p$  range = 0.009 to 0.985) was found between pain and any of the following indices: proprioception, passive ROM, muscle torque, functional ROM and the QoL domains related to social and school functioning. However, a strong negative correlation was observed between knee pain and overall QoL and both physical and emotional functioning ( $r$  range = -0.614 to -0.717; all  $p < 0.001$ ). To date, no investigation was found reporting the relationships between these indices in children with HMS. Because impairments contribute to activity limitations (Stucki and Ewert 2005; Harris et al. 2005), it was thought that there might be strong relationships between pain, muscle torque and functional ROM in children with HMS. However, no correlation was observed between these outcome measures, the reasons for which are not apparent. These findings confirm the results of Sahin et al. (2007) who found no relationship between pain intensity and peak muscle torque in adults with HMS. On the other hand, the significant negative correlation between pain and QoL is very interesting.



The reason for the negative strong correlation between pain and QoL is not known, although it has been suggested that QoL may be of greater importance to individuals with HMS than other variables measured (Ferrell et al. 2004). This may be the case in the present study. This hypothesis is supported by the observation of Ferrell et al. (2004) who found an improved QoL perception with reduced VAS scores following an exercise programme in adults with HMS. Within the present study, a strong negative correlation was observed between impairment and the physical functioning domain of QoL whereas no correlation was found between impairment and functional limitation in these children. The reason for this observation is not known, however, but may be because the functional limitation outcome measure (walking) used in the present study did not involve strenuous and vigorous activities that may result in increased pain perception in children with HMS (Grahame 2000; Adib et al. 2005; Simpson 2006).

In the current study, the correlation between pain and the physical functioning domain of QoL was higher than the other domains (emotional, social and school functioning). Since QoL perception is a measure of well-being, the present results imply that impairments and function are only components of overall well-being in children with HMS.

Although pain may contribute to activity limitations in children with HMS (Gurley-Green 2001; Murray and Woo 2001, Middleditch 2003, Adib et al. 2005), in the present study, there was no direct relationship between the two outcomes. This suggests that pain may not be a good indicator of activity levels in children with this condition. In addition, pain assessment in these children may not reflect their overall neuromuscular impairments. However, it would appear that participation restrictions may be directly related to pain in children with HMS. Therefore, in order to identify the neuromuscular impairments and activity level in children diagnosed with HMS, clinicians are to be aware of these findings and to complement pain measure with other outcomes such as proprioception, muscle torque and gait pattern (functional ROM).

## **8.5 The Relationship between Beighton Scores, Neuromuscular Impairments, Activity Limitations and Participation Restrictions**

Beighton scores are mostly used for assessing GJL and HMS in children (Engelbert et al. 2003; Ruperto et al. 2004). No significant correlation ( $r$  range = -0.098 to 0.337;  $p$  range = 0.074 to 0.895) was found between the Beighton scores and any of the outcome measures assessed as part of the current work (neuromuscular impairments, activity limitations and participation restrictions). The lack of relationship observed between pain and Beighton scores is consistent with the findings of Pountain (1992) and Qvindesland and Jonsson (1999). Milkkelson et al. (1996) found no association between Beighton scores and disability in children with symptomatic GJL (Spearman rank  $r$  = -0.05). They also reported no correlation between knee joint laxity and lower limb pain.

It is believed that some children with GJL do not suffer joint pain (Beighton et al. 1989; Grahame 1990; Grahame et al. 1999; Engelbert et al. 2006). The results of the present study suggest that the presence of neuromuscular impairments may not necessary be related to Beighton scores in children with HMS. In addition, Beighton scores do not reflect the extent of symptoms found in children with HMS. The observations in the present study therefore undermine the value and validity of using a high cut-off point of Beighton scores for assessing HMS in children, as some children with lower Beighton scores could present with important features associated with HMS (such as joint proprioception and muscle weakness) in their lax joints which may not be picked up during assessment. The findings in this study support the notion that the Beighton scores do not give any indication of the severity of the symptoms of HMS (Grahame 1999). Therefore, Beighton scores may not be appropriate for assessing children with HMS but may be a useful starting point for assessing GJL. The current findings therefore, suggest the use of a comprehensive assessment that is capable of identifying the symptoms associated with HMS.

The findings of neuromuscular, functional ROM and QoL indices in healthy children are examined in the next section.

## **8.6 Neuromuscular, Functional ROM and QoL Characteristics in Healthy Children**

This thesis was also aimed at identifying the range of neuromuscular, functional ROM during walking and QoL characteristics in a group of healthy children as information regarding these indices is generally lacking. The normative database of these characteristics has allowed the researcher to identify deviation from normality in children with HMS by comparing their results with those of the healthy children. This section discusses the findings on these indices in healthy children.

The majority of healthy children had zero pain ratings on the coloured analogue scale (CAS), indicating that they had no pain at the time of testing. This observation was expected. However, some healthy girls were found with knee pain during the assessment. Joint laxity may be an underlying risk factor for musculoskeletal pain (Grahame et al. 1999; Adib et al. 2005). Although GJL and the relationship between pain and ROM were not investigated in healthy children in the present study, however, pain experienced by some of the girls may be due to increased knee joint ROM as higher values of both passive extension were observed in girls than boys (Table 7.6). This relationship between pain and ROM in healthy children should be investigated in a future study to confirm such conjecture.

QoL scores in healthy participants were high for each domain and for the overall score. The median values for overall QoL and each of the domains of QoL found in this study were higher than those reported by Varni et al. (2001 and 2004). In the study of Varni et al. (2001), 401 healthy children aged 5-18 years were examined. A research assistant administered the Paediatric Quality of Life Inventory (PedsQL) for children aged 5-7 years whereas older children (8-12 years) and adolescents (13-18 years) were requested to complete the self-report PedsQL. In the current investigation, children aged 8-15 years were examined. While the researcher completed the self-report PedsQL for young children (8-12 years), the adolescents (13-15 years) completed PedsQL by themselves. The higher QoL values obtained in the present study could be because the researcher in the present study filled in the PedsQL for children aged 8-12 years whereas the children did so in the study by Varni et al. (2001). This could have influenced their responses. In addition, the researcher and children found it a bit difficult to interpret the wording of the questionnaire directly. This could also have influenced the children's responses.

Knee joint proprioception was assessed in this study using joint kinaesthesia (JK) and JPS techniques with a purpose-built motorised device. Only the study of Barrack et al. (1983c) was found that investigated knee joint proprioception in children. They investigated JK and JPS in 12 healthy children (mean age = 14.8 years). It is difficult to compare JK findings in the present study with that reported by Barrack et al. (1983c) due to differences in the methods. In addition, the median value of JK was reported in the present study due to the nature of the data whereas Barrack et al. (1983c) presented the mean value in their study. The study of Barrack et al. (1983c) was the first to report JK and JPS in children however their sample size was small ( $n = 12$ ) and limits the generalisability of their findings. The strength of the present study is that it is the first study with a relatively large sample ( $n = 37$ ) that has examined JK and JPS in children. These findings provide reference values for knee proprioception (JK and JPS) in healthy children that can be used for purposes of comparison to identify any deviation from normality in children with pathological conditions.

Knee JPS was assessed in the present study at two different target angles ( $25^{\circ}$  and  $10^{\circ}$ ) with the knee joint passively moved at an angular velocity of  $2.2^{\circ}/s$ . It is believed that these angles are within the working range of the knee during functional and weight-bearing activities (Barrett et al. 1991). A Wilcoxon signed rank test revealed that the AAE obtained in healthy children in the current study was statistically ( $p = 0.034$ ) higher at  $25^{\circ}$  than  $10^{\circ}$  implying that JPS was more accurate at  $10^{\circ}$  than  $25^{\circ}$ . The reason for this is not known, however, this may be related to the capsular ligament tightness at near end ROM as some children anecdotally reported a feeling of tightness at the knee joint during testing at the two target angles. In addition, they stated that tightness was more in the knee joint at test angle  $10^{\circ}$  than  $25^{\circ}$ . This observation was not formally examined in the present study, therefore it is speculation.

This observation supports the theory that joint mechanoreceptors are most sensitive at the terminal range of joint motion (Johansson et al. 1991; Lephart et al. 1992; Borsa et al. 1997). Lephart et al. (1992) suggested that joint angle has a significant effect on the magnitude and frequency of joint mechanoreceptor recruitment. They believed that higher tensile stress is placed on static restraints at end range of motion for knee extension than at mid-ranges of motion. This could have been the

case in the present study. The implication of this finding is that the knee operates close to terminal extension during daily activities, most of which are performed in a weight-bearing position. Therefore, it can be assumed that JPS acuity may be more important at this position. The evidence provided in this thesis suggests that knee JPS should be tested at different ROM angles as the result of JPS at one test angle cannot be used to determine the overall JPS accuracy in children. In addition, JPS tests at near terminal range of motion may be more valuable and clinically relevant.

Knee extensor and flexor muscle torque was measured in the present study using a digital myometer. Muscle torque in children has been reported using different measurement units. For example, muscle torque in children was reported in Newtons (Backman et al. 1989), pounds (Seagraves and Horvat 1995) and kilogrammes (Stuberg and Metcalf 1988). The study of Merlini et al. (1995) who measured muscle torque in Newton meters has an advantage over the investigations of other researchers (Backman et al. 1989; Seagraves and Horvat 1995; Stuberg and Metcalf 1988). The reason for this is already discussed in 8.2.3. Due to lack of standardisation of the measurement units used in previous studies (Stuberg and Metcalf 1988; Backman et al. 1989; Merlini et al. 1995; Seagraves and Horvat 1995), the mean values of muscle torque in the present study could not be compared with their results. A major strength of the present study is that it is the first study to report knee extensor and flexor muscle torque normalised to body mass in healthy children.

Knee flexor muscle torque was found to be approximately half of the extensors in the healthy cohort. This finding is in agreement with the study of Merlini et al. (1995) who examined healthy children aged 6 to 8 years. This study provides an original database on knee extensor and flexor muscle torque in healthy children that can be used to identify potential deficits.

Passive ROM of the knee joint was assessed in the current investigation. There is limited information on passive ROM of the knee joint in healthy children. Boone et al. (1979) examined active knee flexion and extension in 53 healthy boys aged 18 months to 19 years. Although their study provided useful data on knee ROM in children, it is difficult to compare their findings with the results of the present study because the mean value of flexion ROM was reported in their study while the

median value was presented in the current investigation. Additionally, older boys and girls aged 8-15 years were investigated in the current research and passive ROM was assessed in the present study whilst active ROM was tested in that study.

Functional ROM during walking was examined in the present study using the VICON camera system. Again, there is limited information on functional ROM in children. Since it is believed that gait maturation reaches its peak at the age of 8 years (Katoh 1993), functional ROM values in the present study were also discussed in relation to previous studies in adults. The mean values of knee extension in mid-stance and maximum knee flexion observed in the current study agree with the findings of Ounpuu et al. (1991) who examined functional ROM of the knee joint during walking in 31 healthy children (mean age = 9.6 years). In comparison with previous studies in adults, the value ( $60^{\circ}$ ) of maximum knee flexion during walking observed in the present study is similar to that (maximum knee flexion =  $57^{\circ}$ ) reported by Kadaba et al. (1990). The findings of the present investigation further suggest that maximum knee flexion in children 8 years and older approximates that of adults (Katoh 1993). The database of functional ROM during walking in healthy children provided in the present study may be suitable for identifying gait abnormalities in children with pathological gait.

### **8.7 Effect of Gender and Age on Neuromuscular, Functional ROM and QoL Characteristics in Healthy Children**

The effect of gender and age on neuromuscular, functional ROM and QoL characteristics was investigated in healthy children. No gender difference was found between healthy boys and girls in all the indices measured, except for passive knee ROM and the physical functioning domain of QoL. Passive knee ROM was significantly ( $p$  range = 0.015 to 0.020) higher in healthy girls while physical functioning of QoL was significantly ( $p$  = 0.022) poorer in healthy girls than boys. In addition, no age-related difference was found in all the measurement parameters, with the exception of JK, extension ROM, pain and the overall QoL (and emotional, social and school functioning domains of QoL). This is the first study that has examined all of these characteristics in children. One of the aims of this thesis was to investigate age- and gender-related effects on neuromuscular, functional ROM and QoL characteristics in healthy children. Only the measurement variables that were statistically significant are discussed further in this section.

### **8.7.1 Effect of Gender**

Passive ROM (extension and flexion) of the knee joint and the physical functioning domain of QoL were statistically different ( $p$  range = 0.015 to 0.022) between boys and girls. The gender-related difference in passive knee ROM observed in the present study may be the result of deficient ligaments manifesting in joint laxity, which has been found to be more common in girls than boys at any age (Jansson et al. 2004; Gyldenkerne et al. 2007). Hormonal differences between boys and girls may be the reason for the increased ROM in girls than boys. There is evidence to suggest that estrogen and progesterone (female sex hormones) may contribute to increased joint laxity (Heitz et al. 1999). However, neither estrogen nor progesterone levels were examined in the present study. Therefore, the author of this thesis cannot say for sure whether these hormones were responsible for the increased knee ROM found in girls compared with boys. The reason for the significantly poorer physical functioning QoL in girls than boys in the current study is not known. However, it may be because girls and boys handle difficulties and problems differently as girls tend to direct coping patterns inwards and boys outwards (Bissegger et al. 2005). Another explanation could be that girls are more worried and concerned with their health than boys (Bissegger et al. 2005).

### **8.7.2 Effect of Age**

Knee pain, JK, passive extension ROM and overall QoL (including emotional, social and school functioning domains) were significantly different between healthy young children and teenage children in the current investigation. Pain rating was significantly higher in teenagers than younger children. This finding agrees with the observation of Wedderkopp et al. (2005). They found that back pain reported by children increased significantly until the age of puberty. However, the observation in the present study that pain was significantly higher in the teenagers than younger children contrasts with the finding of McGrath et al. (1990) who reported that pain intensity decreased with age, when pain experienced within a period of one month was investigated in healthy children aged 5-17 years using pain diaries. The result of the present study also contrasts with the finding of McGrath et al. (1996). They examined pain intensity in children aged 5-17 years using both CAS and VAS and found an age-related decline in pain intensity on the two scales. The possibility that older children are generally more repeatable in applying a VAS to estimate their pain than younger children (Goodenough et al. 1997) could have accounted for the

higher pain intensity reported by teenage children (as the CAS used in the present study is a modification of the VAS). Therefore, lower pain values reported by younger children may be the result of low between-days repeatability due to random error in pain measurement in these children.

In addition, average pain over a period of one week was examined in the current study. It is possible that memory for pain in younger children was not fully developed compared to their teenage counterparts. This could have led to underestimation of pain experience in the younger children. There is no direct evidence to support these claims however and they require further investigation.

A significant association has been found between high growth spurts and development of musculoskeletal pain in adolescents (Feldman et al. 2001). Therefore, another possible explanation for the increased pain intensity in teenage children compared with younger children may be due to growth spurts that occur during adolescence and may predispose to mechanical micro-trauma (Wedderkopp et al. 2005).

No previous studies were found reporting age differences in knee JK in children. Knee JK was found to be significantly better in teenagers than young children. Although the present results for JK confirm the findings of previous investigations on kinaesthesia in children (Bairstow and Laszlo 1981; Eliot et al. 1988; Hoare and Larkin 1991), it is difficult to make detailed comparison with these studies because of methodological differences. The author of this thesis also recognises that JK of different joints was examined in these studies, further limiting comparison. Given the results of the current study, it can be suggested that knee JK develops with increasing age in children. Additionally, since age-related changes were found in JK but not in JPS, these findings imply that different neuropathways/mechanisms may be responsible for JK and JPS in children. Furthermore, it may also be that the study was underpowered which could have led to statistical aberration.



Passive knee extension ROM was found to be significantly higher ( $p = 0.002$ ) in children than in teenagers. It is believed that joint ROM is inversely related to age in children (Cheng et al. 1991; Flynn et al. 2000). Hence, the age difference in knee extension ROM may be attributed to ligamentous laxity in the young children because joint laxity decreases rapidly during late childhood or early adolescence (Everman and Robin 1998). In addition, age-related decline in joint ROM in children has been suggested to be due to progressive changes in collagen structure that result in stiffening of the connective tissue components of joints (Everman and Robin 1998). However, it is not known why an age-related difference was found in extension ROM and not in flexion ROM. Again, this may be that the investigation was underpowered and therefore the observation calls for further investigation with a larger sample size.

Significantly poorer QoL was found in teenage children compared with their younger counterparts. This finding agrees with the observation of Bissegger et al. (2005) who reported that children had significantly better QoL than teenagers. Although the median values of QoL scores and pain were the same (section 7.5.4) for the young and teenage children, however, the poorer QoL in young children could be the result of pain scores observed in the teenage children as the IQR for pain score was higher in the young than teenage children. This assumption is supported by the observation of Sawyer et al. (2004). They demonstrated that children with higher levels of pain experienced more problems in terms of QoL. This finding may also be because healthy teenagers may be more self-conscious and concerned about their QoL as it relates to physical, emotion, social and school functioning. The present findings on QoL suggest that children with higher levels of pain experience more QoL problems. In addition, separate QoL data for young and teenage children may be required.

In summary, the present results have demonstrated gender-related effects on passive knee ROM (flexion and extension) and the physical functioning domain of QoL. Given these findings, different data on these variables may be required for healthy boys and girls to be able to identify deviation from normality in patients with pathological conditions. In addition, this study has shown the effect of age on passive knee extension, pain, and overall QoL (including emotional, social and school functioning domains). These observations suggest that separate data on

these variables may be necessary for healthy young children and teenagers to enable clinicians to determine any alteration from normal values in children with pathological conditions. Clinicians are to be aware of these findings when making clinical judgments regarding these outcome measures.

The following section examines the relationship between knee JK and JPS in healthy children.

## **8.8 Relationship between Knee JK and JPS in Healthy Children**

The relationship between knee JK and JPS tests has been investigated through studies in healthy adults. The findings of the present study were that there was no correlation between knee JK and JPS at 25°. However, a weak but significant correlation was found between knee JK and JPS at 10°. In addition, a poor relationship was found between the JPS tests at 10° and 25°.

No study was found investigating this matter in children therefore the results of the current investigation were compared with those reported in adults. These findings confirm the observation of Grob et al. (2002) who observed no correlation between knee JK and JPS tests ( $r = 0.20$ ) when they examined 30 healthy subjects (aged 24 to 72 years) using a motorised device. Furthermore, the findings of the present study partly agree with the investigation by Skinner et al. (1984) who found a weak but significant relationship between knee JK and JPS ( $r = 0.293$ ,  $p = 0.025$ ) in 29 healthy subjects (aged 22 to 82 years).

However, the results of this study contrast with the findings of Skinner et al. (1986). They examined the relationship between knee JK and JPS tests before and after fatigue in 11 healthy male volunteers (aged 19 to 28 years) from the US Navy. A strong and statistically significant correlation ( $r = 0.759$ ,  $p = 0.01$ ) was observed between the two measures of proprioception before fatigue. However, a moderate non-significant correlation ( $r = 0.5$ ,  $p = 0.118$ ) was found between these measures after fatigue. Exercise training has been found to improve knee proprioception (Ferrell et al. 2004; Tsang and Hui-Chan 2004; Xu et al. 2004; Sekir and Gür 2005). Therefore, the level of physical activity of the participants in the study reported by Skinner et al. (1986) might have been responsible for their observation. Additionally,

the sample size in Skinner et al.'s study was small and hence their findings could have been due to type I error.

The reason for the lack of correlation between JK and JPS in the present study is not apparent. It is believed that quick-adapting mechanoreceptors such as muscle spindle secondary endings, lamellated corpuscles and Pacinian corpuscles are sensitive to changes in stimulation and are responsible for JK (Lephart et al. 1992; Stillman 2002). JPS is thought to be mediated by slowly adapting mechanoreceptors mainly the primary spindle endings, tendon organs, Ruffini endings and Golgi tendon organs that are maximally stimulated at specific joint angles (Lephart et al. 1992; Stillman 2002). Based on the above, it appears that different sensory receptors may be responsible for JK and JPS. It is believed that both JK and JPS in the lower limb ascends through the spinomedullary tract, which is in the posterolateral white matter that overlaps the dorsal spinocerebellar tract (Tortora and Grabowski 2003), however, due to the lack of correlation between these tests (JK and JPS) it seems that different central proprioceptive neuropathways may be responsible for them. Alternatively, it is possible that the interpretation of JK versus JPS in the brain is based on the different patterns and frequencies of impulses propagated by the same nerves. These hypotheses are mere speculations, as there is no evidence to support them and can serve as area of further investigation.

These findings suggest that clinical judgement should not be based on independent tests of either JK or JPS as they may be assessing different components of proprioception which may be important. Therefore, they provide justification for continual use of both tests for knee proprioception assessment.

## 8.9 Overall Summary of Discussion

This chapter has discussed the results of neuromuscular, functional ROM and QoL characteristics in children with HMS and healthy children. In the present investigation, the level of neuromuscular impairments, functional ROM and QoL in children with HMS have been identified and presented. While examining the relationship between pain, neuromuscular impairments, functional ROM and QoL characteristics in these children, it was found that a strong relationship existed between pain and the level of QoL in children with HMS. In the present study, no correlation was observed between pain and neuromuscular and functional ROM indices in children with HMS. In addition, no relationship was found between Beighton scores and neuromuscular, functional ROM and QoL indices in children with HMS.

Gender- and age-related patterns of some of the indices (that were statistically significant) have been discussed in healthy children. Caution must be exercised in the interpretation of the current findings on gender- and age-related changes in healthy children due to the small sample size for this sub-group analysis. However, these observations suggest that separate data of ROM and physical functioning domain of QoL may be required for boys and girls for determining ROM limitation and the level of QoL (physical functioning) in children with pathological conditions in comparison with their healthy counterparts. In addition, these findings also imply that different clinical data on knee pain, JK, extension ROM and overall QoL (including emotional, social and school functioning domain) may be necessary for young and teenage children to identify those with pathological conditions. No correlation was found between proprioceptive outcome measures (JK and JPS) in healthy children suggesting that each proprioceptive technique may be measuring different components of joint proprioception that might be important and that the results of one test cannot be used to determine the overall joint proprioceptive ability in children. Hence, further use of both knee JK and JPS tests is encouraged.

In conclusion, it has been demonstrated in this thesis that children with HMS had neuromuscular impairments (JK, JPS and muscle torque), and reduced knee flexion and increased knee extension during walking. Additionally, these children had a poorer QoL and increased pain perception. These findings therefore imply that neuromuscular impairments, activity limitations and participation restrictions may be found in children with HMS. Many studies have focused on pain, while few investigations have been carried out to examine muscle torque in children with HMS and other symptoms have been neglected. This may affect the quality of treatment received by children with HMS as important factors may not be identified. The advantages of the present study are that it has identified a range of signs and symptoms associated with HMS in children. It has also determined the level of neuromuscular impairments, functional ROM and QoL characteristics in healthy children. Therefore, the findings of the present study provide original data with which future studies on these indices can be compared.

The following chapter discusses the summary and recommendations of this study.

## **CHAPTER 9 : SUMMARY, RECOMMENDATIONS AND CONCLUSIONS**

### **9.1 Introduction**

The knowledge, identification and quantification of neuromuscular impairments, functional ROM and quality of life (QoL) measures in children with HMS have been limited by lack of published results. The use of the newly developed motorised device and a range of outcome measures in the present work has already been discussed (chapter 8). The advantages and the disadvantages of the outcome measures have also been examined. The present researcher has identified some specific impairments, activity limitations and participation restrictions in children with HMS that may prove important in informing the treatment of this condition. This chapter presents the summary of the findings, recommendations and conclusions drawn from the present investigation.

### **9.2 Summary**

#### **9.2.1 Findings of the Study**

The main aim of this thesis was to identify the neuromuscular performance, functional ability and QoL characteristics of children diagnosed with hypermobility syndrome (HMS). A summary of the findings related to the aims of the present study (see section 1.2) are presented in this section.

#### **9.2.2 Aims of the Study**

##### **Primary Aims**

1. The neuromuscular performance, functional ROM and QoL characteristics were identified and quantified in 29 children with HMS by comparing them with 37 healthy non-symptomatic children. The findings showed that children with HMS had neuromuscular impairments, activity limitations and participation restrictions compared with their healthy counterparts.
2. No relationship was found between the different neuromuscular impairments assessed (pain, JK, JPS, passive ROM and muscle torque) in children with HMS. Also, no correlation was observed between pain and activity limitations (functional ROM during walking) in these children. However, a strong negative relationship was established between pain and participation restrictions (QoL) in children with HMS.

## **Secondary Aims**

1. A new device for assessing knee joint proprioception was developed and validated. This device provided a quantitative measure of joint kinaesthesia (JK) and joint position sense (JPS) of the knee joint in healthy children and those with HMS. The criterion-related validity of lower leg displacement when placed in the purpose-built motorised device was excellent. This suggests that the purpose-built motorised device has the potential of providing quantifiable proprioceptive data in these children. The between-trials repeatability of the motorised device indicated that learning effects occurred in healthy subjects when used to assess knee JPS. As a result, this phenomenon was considered when designing a protocol for assessing knee JK and JPS in this research.
2. The test-retest/intra-rater repeatability of a range of the outcome measures used for assessing the neuromuscular performance, functional ROM and QoL characteristics was investigated in healthy children and those diagnosed with HMS. Using ICC and 95% limits of agreement (LOA) it was found that the test-retest/intra-rater repeatability of all the measurement parameters in healthy children and those with HMS was excellent except for JPS and functional ROM assessments. The possible reasons for the low repeatability of these outcome measures were discussed in section 6.5. These outcome measures have the potential of being used for assessing and planning of therapeutic intervention in children with this condition.
3. Healthy girls were found to have a statistically significant increased passive knee ROM (extension and flexion) and poorer QoL (physical functioning domain) than healthy boys. In addition, healthy teenage children exhibited statistically significant increased pain perception, reduced knee extension ROM, poorer knee joint proprioception (JK) and poorer overall QoL (including emotional, social and school functioning domains) than the healthy young children.
4. No statistically significant correlation was found between JK and JPS in healthy children.

### **9.2.3 Summary of Clinical Implications**

Analysis of the literature (chapter 2) revealed that the majority of studies conducted on musculoskeletal complaints in children with HMS have focussed on pain (Adib et al. 2005), muscle torque (Engelbert et al. 2003; 2004; 2006) and motor development (Jaffe et al. 1988; Engelbert et al. 2005). No studies were found on joint proprioception, functional ROM during walking and QoL in children with HMS. It was therefore concluded that there was a lack of adequate knowledge of the possible features associated HMS in children. This thesis has identified a range of signs and symptoms in children with HMS.

The present investigation demonstrated that there were a number of neuromuscular impairments (pain, JK, JPS and muscle torque) associated with HMS in children. In addition, passive joint ROM of the knee joint and knee extension during walking was observed to be higher in these children. They also had reduced knee flexion during walking and a poorer level of QoL. These findings therefore imply that HMS is a multifactorial disorder that is associated with a range of neuromuscular impairments, activity limitations and participation restrictions. These findings also highlight the limitation of the Beighton scores, the most commonly used method for defining HMS in children as they were only designed to identify pain and GJL. As the aim of physiotherapy treatment in these children and any other patients should be based on the clinical diagnosis and findings, accurate and comprehensive assessment is required.

It is acknowledged that there may be other factors associated with HMS that have not been measured in the present study, however, in order for children with this condition to receive appropriate treatment for their condition, the identified symptoms (section 8.2) are to be examined. Reduced knee pain and ROM was reported in patients with HMS following a six week exercise programme (Barton and Bird 1996). Ferrell et al. (2004) also found that knee joint pain, JK, muscle torque, balance and QoL improved with closed kinetic exercise in patients with HMS. In addition, Ferrell et al. (2007) observed an improvement in musculoskeletal reflex in patients with HMS following an 8-week close kinetic exercise programme. Therefore, children with HMS may benefit from physiotherapy treatment such as muscle strengthening and proprioception enhancement programmes. Children with this condition may also benefit from treatment directed towards pain management



and walking re-education. QoL management such as advice and counselling may also be of value to children with HMS (Murray and Woo 200; Middleditch 2003; Murray 2006; Bird 2007).

Given the multifactorial nature of the symptoms associated with HMS and the evidence provided in support of their possible management, it seems likely that effective management of children with this condition would require a multidisciplinary approach.

There was a lack of correlation between pain, other neuromuscular impairments and activity limitations in children with HMS. This could indicate that pain experienced by children with HMS in the present study may not necessarily be related to these outcomes (neuromuscular impairments and functional ROM) or vice versa in children with HMS. It can therefore be concluded that the level of pain experienced by children with HMS cannot be used to determine the overall level of impairments and activity limitation in children with HMS. However, given the findings of the present study on the range of signs and symptoms associated with HMS, neuromuscular impairments and activity limitations are separate outcomes, that may also be important during the assessment of children with this condition. On the other hand, the strong relationship observed between pain and participation restrictions (poorer QoL) could suggest that the poorer QoL in children with HMS may be due, in part, to pain experienced by the children. This therefore suggests that appropriate pain management in children with this condition is vital as this would not only help to reduce pain but improve the level of participation of children with HMS. Finally, given that this thesis is the first to investigate these range of symptoms in children with HMS, its findings can be used for comparison with future studies of HMS in children.

Repeatability tests in healthy children (Table 6.2) and those with HMS (Table 6.3) revealed that all the outcome measures can be used with high between-days repeatability, except for the JPS and knee kinematics. Hence, such outcome measures could be used to identify the level of neuromusculoskeletal impairments and thereby influencing treatment plans for children with HMS. JPS and kinematics data in these children should be used with prudence. The learning effects found during JPS testing implies that adequate familiarisation with the JPS test procedure is required when using a purpose-built motorised apparatus. The findings in healthy

children revealed that different clinical data on passive ROM and the physical functioning domain of QoL may be necessary for boys and girls, rather than considering all data together. It also appears that different data for pain, passive knee extension, JK and overall QoL (including emotional, social and school functioning domains) may be required for young children and teenage children.

Furthermore, the weak relationship found between knee JK and JPS tests in this study could mean that each test assesses different components of proprioception and does not represent the overall joint proprioceptive ability in individuals. It also implies that different sensory receptors and neuropathway/mechanisms may be responsible for JK and JPS. The poor relationship observed between the JPS tests at the two test angles ( $25^{\circ}$  and  $10^{\circ}$ ) suggests that different structures may be responsible for JPS at these test angles. The implication of these findings is that caution must be taken in interpreting either the results of knee JK or JPS tests, as the findings of one proprioceptive test cannot be substituted for the other. In addition, JPS test assessment at different test angles may be required. Therefore, clinical judgement on the overall joint proprioceptive accuracy in individuals should not be based on, for example, examination of JPS at one target angle. Clinicians should be aware of these findings and should not make clinical judgements based on independent tests of either joint JK or JPS. These findings provide justification for continual use of both tests for knee proprioception assessment as they may be assessing two different proprioceptive systems, both of which might be important for normal function.

### **9.3 Strengths and Limitations of the Outcome Measures**

In the present study, the outcome measures used in the present study were designed in response to the need for quantitative methods to identify and quantify neuromuscular impairments, functional ROM and QoL measure in children with HMS. Any assessment method has inherent strengths and limitations and these are examined in this section.

A number of neuromuscular indices such as pain, JK, JPS, muscle torque and ROM were included in this assessment method. The method also consisted of comprehensive assessment of QoL in children that covered four domains (physical, emotional, social and school). The assessment method used in the present study included function and QoL measures. In terms of clinical implications this is a major

advantage as many diagnostic criteria (such as the Carter and Wilkinson criteria, Beighton score and Brighton criteria) currently being used in clinical practice are subjective and do not include any measure of function and QoL. The assessment methods used in the present study may be used for planning appropriate physiotherapy treatment.

This thesis is the first that has examined a wide range of neuromuscular, functional ROM and QoL characteristics in children with HMS and their healthy counterparts. It involved 29 children with HMS aged 8 to 15 years. The sample size in the present study was appropriately powered on the basis of pilot work (section 5.10). This sample size is relatively larger than the studies of Engelbert et al. (2003; 2004; 2006) who studied 15, 19 and 13 children with HMS respectively. Moreover, the sample size used in the current investigation is larger than previous investigations where knee JK was examined in 10 (Hall et al. 1995) and 18 (Ferrell et al. 2004) adults with HMS. This further provides evidence in support of the originality of the present study and making it another major strength of this thesis.

One major disadvantage of the assessment methods used in the present work was the time required for children to complete the assessment tasks, (approximately 90 minutes). Taking child protection law into consideration no child was seen without the parent or an accompanying adult present during the assessment. The assessment was time-consuming for all concerned, making it difficult to use routinely in clinical practice. In addition, the method included only one functional task (functional ROM during walking), and may not reflect the overall functional ability of children with HMS. The clinical study carried out in this thesis involved 37 healthy children (20 boys and 17 girls) and 29 children with HMS (8 boys and 21 girls). A sample with more boys with HMS would have been preferable, particularly for the purpose of generalisability and investigation of age- and gender-related effects on the findings in this study.

The digital myometer and VICON system are expensive and may not be available for routine clinical use. Additionally, functional ROM data processing on the VICON was time-consuming. The QoL inventory questionnaire used in the present study had a 5-point Likert scale. On inspection of the raw data, it was observed that the HMS participants' responses were mainly around the middle point (3). It is possible

that the participants' responses were influenced by the number of points on the scale as they may not want to score high or low on the QoL questionnaire. This might not reflect the actual level of QoL in children with HMS.

JK and JPS were tested using a purpose-built motorised device. This is another major advantage of the present research, as no other studies were found investigating these two measures of proprioception in a group of patients with HMS. This has the advantage of providing quantifiable data on different components of proprioceptive ability in children with HMS. This device has the potential to be used for assessing joint proprioception in patients with HMS who may have pain (Everman and Robin 1998; Adib et al. 2005; Ferrell et al. 2007; Sahin et al. 2007) and impaired muscle function (Middleditch 2003; Adib et al. 2005), as these may affect participants' ability to generate muscle force required for active JPS test. The testing was non-invasive, easy to implement and not distressing to children or their parents. All these advantages combined to provide proprioceptive measures (JK and JPS) that are reflective of physiotherapy assessment and treatment in children with HMS.

The purpose-built motorised device used for measuring knee JK and JPS in the current study had the following limitations: (i) The stepper motor of the device was noisy which could be a source of distraction to participants during testing; (ii) The device was big, cumbersome and required a large amount of space making it inappropriate for routine clinical use; (iii) The device had a maximum angular velocity of  $2.2^{\circ}/s$ , therefore it was not possible for subjects' limb to be moved at a faster angular velocity. In order for these limitations to be addressed, future research should be aimed at designing a portable and sound proofed motorised device for assessing knee JK and JPS. Additionally, future development of a purpose-built motorised device should take into account of a faster angular velocity than that which was used ( $2.2^{\circ}/s$ ) in the present study. This will allow the participants' limb to be passively moved at higher angular velocity which may reflect the way the knee joint moves during functional activities. Furthermore, such a device could be developed and made available commercially.

There was no blinding during data collection in the present study (healthy children and HMS) and this could have led to bias on the part of the researcher. The author of this thesis acknowledges the importance of blinding in a clinical study. However, due to the nature of the research, it was not possible for blinding to be carried out. For instance, the researcher needed to know which subject was being tested as the test knee was determined in randomised order in healthy children using computer randomisation, whereas the more painful knee was tested in children with HMS. If there was blinding, it could have been difficult for the researcher to implement alone without having to employ an assistant. Other limitations to the present study are presented below.

- A cross-sectional design was used in the present study, which only allowed identification of the factors associated with HMS in children and the relationships between them. Therefore, no firm conclusions could be drawn on the cause and effect relations of the impairments, activity limitations and participation restrictions observed in children with this condition.
- The relationship between pain, neuromuscular impairments, activity limitations and participation restrictions was investigated at one time, therefore, it does not provide information about which outcome might be more responsive to change in children with HMS.
- Pain assessment was carried out only once in this thesis, therefore, pain intensity observed in these children may not be reflective of their pain experience as there could have been pain fluctuation in children with HMS. In addition, pain intensity in children with HMS may not be accurate as some of these children were undergoing treatment at the time of assessment.
- Only the knee joint was examined in the present study therefore the findings may not be applicable to other joints.
- The QoL questionnaire was completed by the researcher (for children aged 8 -12 years) in the present study and the researcher found it difficult to

interpret the wording of the questionnaire directly. Therefore, the level of QoL reported by children (healthy and HMS) may not be accurate.

- Generalised joint laxity was not examined in healthy children. Hence, the level of pain found in some healthy children could have been due to GJL.
- The criterion-related validity of angular displacement of the proprioception device was not investigated, making it a limitation of the present study. Further research should therefore be carried out to investigate the criterion-related validity of the angular displacement of the device.

In conclusion there are strengths and limitations of the assessment method used in this thesis. It is evident that the major strengths of these quantitative outcome measures lie in their ability to measure a wide range of neuromuscular impairments, activity limitations and participation restrictions in children with HMS. This method could be used for clinical assessment of children with HMS. However, a major drawback of the assessment method was that it was time-consuming to administer. It is envisaged that the limitations discussed could be addressed in future studies of children with HMS.

Although it was demonstrated that there were significant differences in all the outcomes included in the present study, however, it is likely that some of these outcomes might be more important than others. Therefore, to establish the signs and symptoms that might be important in children with HMS, the predictive validity of the features should be identified through a study investigating their responses to appropriate intervention.

## **9.4 Recommendations**

### **9.4.1 Purpose-Built Motorised Testing Device**

The following are recommendations for future studies on the purpose-built proprioception testing device:

- To investigate the criterion-related validity of the angular displacement of the knee joint using the proprioception testing device in healthy children and those diagnosed with HMS.
- To examine the test-retest repeatability of knee flexion-extension axis identification in healthy children and those with HMS.
- To determine the inter-rater repeatability of the purpose-built testing device.
- To develop a more sensitive method of measuring knee angular displacement (as opposed to the protractor) on the motorised device during JK and JPS assessment using the motorised device.
- To develop a bigger and more comfortable lower limb support for the proprioception testing apparatus that can be used in children and adults.
- To investigate the effect of duration of testing and cognitive distraction on joint proprioception testing in children.

### **9.4.2 Assessment Method Used in the Present Study**

The following are suggested to improve the assessment methods used in the present study.

- To include some more functional tasks that reflects the overall functional ability in children with HMS.
- To determine the inter-rater repeatability of the methods in both healthy children and those with HMS.
- To establish the responsiveness of the methods following a treatment intervention in children with HMS.

### **9.4.3 Suggestions for Future Research using the Assessment Method**

Future research investigations are required to identify the signs and symptoms in younger and older children than those studied in the present research, using this assessment method. Although there were significant differences in each of the measures, the gender imbalance in the sample used could not permit the researcher to investigate in detail the influence of age and gender on the measurement variables, which may help to improve the knowledge of the underlying basis of the

symptoms associated with HMS in children. In view of the fact that the present study was limited to the knee joint, future studies are required to examine these features in relation to other symptomatic joints in children with HMS and to develop appropriate treatment interventions.

Given the findings of the present research, neuromuscular impairments, functional ROM during walking and QoL assessment may be incorporated into routine clinical examination of children with HMS. It may be important for clinicians and researchers to be aware of the identified signs and symptoms in children with HMS.

Due to the cross-sectional design used in the present study the cause and effect relations of the neuromuscular impairments, activity limitations and participation restrictions in children with HMS could not be ascertained, therefore, future studies with longitudinal designs are needed to be able to draw more firm conclusions.

## **9.5 Overall Conclusions**

In comparison with healthy children, the following signs and symptoms were identified in children with HMS in the present study:

- Increased pain perception
- Impaired knee joint proprioception (JK and JPS)
- Reduced knee extensor and flexor muscle torque
- Increased passive knee joint ROM (extension and flexion)
- Increased knee extension and reduced knee flexion during walking
- Poorer QoL perception (including physical, emotional, social and school functioning domains)

These findings therefore imply that HMS in children is a multi-faceted condition affecting neuromuscular impairments, activity limitations and participation restrictions. Therefore, intervention programmes for children with HMS should be both multidisciplinary and multi-dimensional, aiming to alleviate the neuromuscular impairments, improve activity levels and enhance the participation levels in children with this condition.



This thesis also found that the Beighton scores commonly used for assessing HMS can only be used to identify GJL and pain as they do not give indication of other important symptoms that may be found in HMS. Therefore, Beighton scores should be complimented with a more comprehensive assessment that has the potential of identifying the level of activity limitation and participation restriction in children with this condition. The lack of relationship between the two measures of joint proprioception supports their continued use as separate outcomes for measuring proprioceptive acuity.

The evidence reported in this thesis has added distinctly to the current knowledge of clinicians in terms of neuromusculoskeletal impairments, functional ROM and QoL in children with HMS. Identifying these features could help to guide the appropriate treatment for children with this condition.

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## APPENDICES

### Appendix 1: Summary of the results of bench validation and repeatability experiments on digital myometer and universal goniometer

Experiments	ICC	95% LOA
Criterion-related validity of force measurements by digital myometer against weighing scale (N)	1.00	-2.45 to 3.35
Within-day repeatability of digital myometer (N)	0.98	-2.04 to 3.58
Between-days repeatability of digital myometer (N)	0.95	-2.9 to 3.20
Criterion-related validity of angular measurements of the universal goniometer myometer against Myrin goniometer ( <sup>0</sup> )	0.97	-0.12 to 0.09
Within-day repeatability of universal goniometer ( <sup>0</sup> )	0.95	-0.32 to 0.29
Between-days repeatability of universal goniometer ( <sup>0</sup> )	0.92	-3.35 to 4.29

Keys:

ICC = Intraclass correlation coefficients

LOA = Limits of agreement

N = Newtons

<sup>0</sup> = degree

## Appendix 2a

ID#	_____
Date:	_____

# PedsQL<sup>TM</sup>

## Paediatric Quality of Life Inventory

Version 4.0 – UK English

**CHILD REPORT** (ages 8-12)

### DIRECTIONS

On the following page is a list of things that might be a problem for you.  
Please tell us **how much of a problem** each one has been for you  
during the **PAST MONTH** by circling:

- 0 if it is **never** a problem
- 1 if it is **almost never** a problem
- 2 if it is **sometimes** a problem
- 3 if it is **often** a problem
- 4 if it is **almost always** a problem

There are no right or wrong answers.  
If you do not understand a question, please ask for help.

In the **PAST MONTH**, how much of a **problem** has this been for you ...

<b>ABOUT MY HEALTH AND ACTIVITIES (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. It is hard for me to walk more than a couple of streets (about 100 metres)	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activities or exercise	0	1	2	3	4
4. It is hard for me to lift heavy things	0	1	2	3	4
5. It is hard for me to have a bath or shower by myself	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I have aches and pains	0	1	2	3	4
8. I feel tired	0	1	2	3	4

<b>ABOUT MY FEELINGS (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

<b>HOW I GET ON WITH OTHERS (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. I have trouble getting on with other children	0	1	2	3	4
2. Other children do not want to be my friend	0	1	2	3	4
3. Other children tease me	0	1	2	3	4
4. I cannot do things that other children my age can do	0	1	2	3	4
5. It is hard to keep up when I play with other children	0	1	2	3	4

<b>ABOUT SCHOOL (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my schoolwork	0	1	2	3	4
4. I miss school because of not feeling well	0	1	2	3	4
5. I miss school to go to the doctor or hospital	0	1	2	3	4



## Appendix 2b

ID#	_____
Date:	_____

# PedsQL<sup>TM</sup>

## Paediatric Quality of Life Inventory

Version 4.0 – UK English

### TEENAGER REPORT (ages 13-18)

#### DIRECTIONS

On the following page is a list of things that might be a problem for you.  
Please tell us **how much of a problem** each one has been for you  
during the **PAST MONTH** by circling:

- 0 if it is **never** a problem
- 1 if it is **almost never** a problem
- 2 if it is **sometimes** a problem
- 3 if it is **often** a problem
- 4 if it is **almost always** a problem

There are no right or wrong answers.  
If you do not understand a question, please ask for help.



In the **PAST MONTH**, how much of a **problem** has this been for you ...

<b>ABOUT MY HEALTH AND ACTIVITIES (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. It is hard for me to walk more than a couple of streets (about 100 metres)	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activities or exercise	0	1	2	3	4
4. It is hard for me to lift heavy things	0	1	2	3	4
5. It is hard for me to have a bath or shower by myself	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I have aches and pains	0	1	2	3	4
8. I feel tired	0	1	2	3	4

<b>ABOUT MY FEELINGS (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

<b>HOW I GET ON WITH OTHERS (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. I have trouble getting on with other teenagers	0	1	2	3	4
2. Other teenagers do not want to be my friend	0	1	2	3	4
3. Other teenagers tease me	0	1	2	3	4
4. I cannot do things that other teenagers my age can do	0	1	2	3	4
5. It is hard to keep up with other teenagers my age	0	1	2	3	4

<b>ABOUT SCHOOL / COLLEGE (problems with...)</b>	Never	Almost Never	Some-times	Often	Almost Always
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my school / college work	0	1	2	3	4
4. I miss school / college because of not feeling well	0	1	2	3	4
5. I miss school / college to go to the doctor or hospital	0	1	2	3	4

### Appendix 3.1: Letter of Invitation to Participate in the Study



St Mary's (Leith) RC Primary  
Links Gardens Edinburgh EH6 7JG

Tel 0131 554 7291  
Fax 0131 554 8523

Headteacher Mary F Clason Dip CE AUPE

Dear Parent

**Researchd Project: Developing an Assessment Strategy for Children diagnosed with Hypermobility Syndrome**

A post graduate student in Physiotherapy at Queen Margaret College situated across from our school has asked the Authority and me if he could recruit healthy Scottish children from our school who may be interested in taking part in the above research.

This would involve your child attending the human performance laboratory at Queen Margaret College, Leith Campus, on one occasion for about one hour.

Please sign below if you are interested and the research student will send out a letter with further information.

Yours sincerely

Mary F Clason  
Headteacher

✂-----  
**Research Project: Developing an Assessment Strategy for Children diagnosed with Hypermobility Syndrome**

Name of Pupil \_\_\_\_\_ Class \_\_\_\_\_

I am interested in hearing more about this research project.

Signature of Parent/Guardian \_\_\_\_\_ Date \_\_\_\_\_

• EDINBURGH •  
THE CITY OF EDINBURGH COUNCIL

EDUCATION

### Appendix 3.2: Letter of Invitation to Participate in the Study



THE CITY OF EDINBURGH COUNCIL

Education Department

4<sup>th</sup> October 2004

Dear Parent

**Research Project: Developing an Assessment Strategy for Children diagnosed with Hypermobility Syndrome**

A post graduate student in Physiotherapy at Queen Margaret College situated across from our school has asked the Authority and me if he could recruit healthy Scottish children from our school who may be interested in taking part in the above research.

This would involve your child attending the human performance laboratory at Queen Margaret College, Leith Campus, on one occasion for about one hour.

Please sign below if you are interested and the research student will send out a letter with further information.

Yours sincerely

A handwritten signature in black ink, appearing to read "Christine Rose".

Christine Rose  
Head Teacher

✂-----

**Research Project: Developing an Assessment Strategy for Children diagnosed with Hypermobility Syndrome**

Name of Pupil .....

Class -----

I am interested in hearing more about this research project.

Signature of Parent/Guardian .....

Leith Primary School  
St. Andrew's Place Leith Edinburgh EH6 7 Tel 0131 554 4844 Fax 0131 467 7988

Email: [admin@leith-pri.edin.sch.uk](mailto:admin@leith-pri.edin.sch.uk)  
Website: [www.leith-pri.edin.sch.uk](http://www.leith-pri.edin.sch.uk)

### Appendix 3.3: Letter of Invitation to Participate in the Study



Queen Margaret University College  
EDINBURGH

Francis Fatoye  
Research Student  
Edinburgh, EH6 8HF  
Tel: 0131 317 3665  
Fax: 0131 317 3815  
Email: [ffatoye@qmuc.ac.uk](mailto:ffatoye@qmuc.ac.uk)

Date

Dear Parent,

**Research Project: “Developing an Assessment Strategy for Children Diagnosed with Hypermobility Syndrome (HMS)”**

Thank you for your interest in the above research study. I am writing this letter as a follow up to the letter you received from your child's head teacher regarding my study. I am a chartered Physiotherapist and post-graduate research student in Physiotherapy at Queen Margaret University College (QMUC), Edinburgh. This study is being conducted with the approval of the Education Department, City of Edinburgh Council and your child's head teacher.

Enclosed is a copy of the information sheet, response sheet, two copies of the parental consent form and two copies of the participant (your child's) consent form. If you consent to your child taking part in this study then please complete the response sheet and the consent forms **(one signed copy of each of the consent forms to be retained by you and one signed copy of each of the consent forms to be returned with the response sheet in the pre-paid envelope to Francis Fatoye)**

On receipt of the forms I will contact you in order to answer any questions that you/your child may have concerning the study and to make the necessary arrangements for your child's visit to QMUC. Alternatively you can contact me directly at the above address.

Yours sincerely,

Francis Fatoye MSc MCSP  
Research Student  
Enc.

## Appendix 3.4: Response Sheet



Queen Margaret University College  
EDINBURGH

**Confidential**

### Response sheet

#### Developing an Assessment Strategy for Children Diagnosed With Hypermobility Syndrome (HMS)

Yes, I am happy for **Francis Fatoye** to contact me about this project

Name of parent/guardian (in block letters).....  
Address.....  
.....  
Post  
code.....  
Telephone number (Day) ..... (Evening).....  
Best time to call.....  
Email  
(optional).....  
Child's name.....  
Child's ..... age  
.....  
Parent/guardian's signature ..... Date  
.....

**Please return this response sheet and the signed consent forms in the pre-paid envelope provided**

Contact details  
Phone: 0131 317 3665  
Email: [ffatoye@qmuc.ac.uk](mailto:ffatoye@qmuc.ac.uk)

## Appendix 3.5: Information sheet for Healthy Children



Queen Margaret University College  
EDINBURGH

### Information Sheet for Healthy Children

#### Study Title

#### **“Developing an Assessment Strategy for Children Diagnosed with Hypermobility Syndrome (HMS)”**

Thank you for your interest in this research study. Before you decide if you would like your child to take part it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following carefully and discuss with others if you wish. If there is anything that is not clear or you would like more information please contact me at the number below.

#### **What is the purpose of the study?**

Joint laxity is an increase in joint range of motion beyond that which is considered normal. Hypermobility syndrome (HMS) is a generalised joint laxity with associated musculoskeletal (muscles and bones) complaints in otherwise normal subjects. Children with HMS are often not diagnosed and they do not receive appropriate treatment for their condition, because there is no scientific and comprehensive method of assessing the symptoms associated with their condition. The relationship between generalised joint laxity and neuromusculoskeletal (nerves, muscles and bones) complaints in children is not understood. There is limited published data on the range of neuromusculoskeletal (nerves, muscles and bones) complaints and the level of quality of life in healthy children and children with HMS. The relationships between symptoms and their implications for functional ability and quality of life are also currently unknown in children with HMS. The purpose of this study is to understand the level of impairments and quality of life associated with HMS by developing a scientific and comprehensive assessment strategy of neuromusculoskeletal (nerves, muscles and bones) impairments and quality of life for children diagnosed with HMS, that can be used for assessment and planning of an intervention strategy.

#### **Why has your child been chosen?**

Your child has been chosen because he/she is healthy and he/she is within the ages of 8-15 years. We need to determine the normal functions of the nerves, muscles and bones and the level of quality of life in healthy Scottish children. Comparison of the problems in children diagnosed with HMS with the data for healthy children will allow us to establish the severity of their condition. Parents of 25 healthy children in the city of Edinburgh are being approached to allow their children to participate in this study.

**Do I have to allow my child to take part?**

It is up to you to decide whether or not to allow your child to take part. You do not need to give a reason if you decide not to allow your child to take part in the study. If you decide to allow your child to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to allow your child to take part you are free to withdraw your child from the study at any time without giving a reason.

**What will happen to my child if I allow him/her to take part?**

Your child will report once to the QMUC human performance laboratory, 89 Duke Street, Leith in gym shorts and t-shirt. A brief explanation of the procedure will be given to the child and his/her weight and height will be recorded. He/she will undergo the following measurements: knee joint range of motion will be assessed using a device that measures joint angles, the average pain (if any) felt by your child over the last week will be assessed using a coloured scale like a ruler, knee joint position sense will be assessed using a device that moves the leg slowly and gently, muscle strength will be assessed with a small portable machine and the functional range of motion and walking pattern will be assessed using a camera system. Quality of life will be assessed with a questionnaire. Both knees will be tested twice. The whole procedure will take approximately 1 hour.

**What does my child have to do?**

The only thing your child has to do by taking part is to report to the human performance laboratory of the Queen Margaret University College Edinburgh, and undertake the procedures outlined above. There is no other requirement.

**What are the possible disadvantages and risks of my child taking part?**

There are no possible disadvantages of your child taking part in the study as it involves non-invasive, simple and safe clinical assessments, as would be completed during a routine physiotherapy assessment. However, there are minimal risks to your child in taking part in the study such as a possible fall or trip. Risk assessment of the human performance laboratory has been carried out to minimise these risks during your visit. Queen Margaret University College has a public liability insurance scheme for compensation as a result of harm caused due to negligence on the part of the researcher in connection with the above mentioned study.

**What are the possible benefits of my child taking part?**

The study will produce no direct benefit to your child. However, your child's participation in this research will provide the opportunity for him/her to experience how his or her joints and muscles work, learn about joint position sense (proprioception) and to know about his or her quality of life. The information we will obtain from the study will help us to identify the symptoms associated with HMS in other children and to develop a scientific and comprehensive method of assessing children with HMS.

**Will my child's taking part in this study be kept confidential?**

All information which is collected about your child will be kept strictly confidential. Any information about your child which leaves the premises will have your child's name and address removed so that they cannot be recognised or identified.

**What will happen to the results of the research study?**

The results of the research will be published some months after the study has been completed. The results will be published as research papers in scientific journals and will also be available as part of a research thesis at the Queen Margaret University College library. Your child will not be identified in any of the reports or medical publications and all data will only be kept until the study and all associated works are completed.

**Who is organising and funding the research?**

Francis Fatoye, a research student based at the Leith campus of the Queen Margaret University College in Edinburgh, is conducting this study. Queen Margaret University College funds the study as a PhD research degree.

**Thank you for taking the time to read this information sheet. If you or your child have any questions please do not hesitate to contact Francis Fatoye during office hours.**

**Mr Francis Fatoye MSc MCSP  
PhD Student  
Physiotherapy Subject Area  
Queen Margaret University College  
89 Duke Street  
Edinburgh  
EH6 8HF  
Tel: 013 1317 3665  
E-mail: [ffatoye@qmuc.ac.uk](mailto:ffatoye@qmuc.ac.uk)**

**INDEPENDENT CONTACT  
Dr Fiona Macmillan PhD MCSP  
Head of Physiotherapy  
Queen Margaret University College  
89 Duke Street  
Edinburgh  
EH6 8HF  
0131 317 3640  
E-mail: [fmacmillan@qmuc.ac.uk](mailto:fmacmillan@qmuc.ac.uk)**



### Appendix 3.6: Parental Consent Form (Healthy Children)



Queen Margaret University College  
EDINBURGH

Subject's Identification Number:

#### PARENTAL CONSENT FORM

**Title of Project:**

**Developing an Assessment Strategy for Children Diagnosed with  
Hypermobility Syndrome (HMS)**

**Name of Researcher:** Francis Fatoye

Please initial box

I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions.

☐

I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reason, without his/her legal rights being affected.

☐

I agree for my child (.....) to participate in the above study

☐

\_\_\_\_\_  
Name of Child's parent/guardian  
in capital letters

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of person taking consent  
(if different from researcher)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

1 for parent/guardian and 1 for researcher

### Appendix 3.7: Participants Consent form (Healthy Children)



Queen Margaret University College  
EDINBURGH

Subject's Identification Number:

#### PARTICIPANT CONSENT FORM

**Title of Project:**

**Developing an Assessment Strategy for Children Diagnosed with  
Hypermobility Syndrome (HMS)**

**Name of Researcher:** Francis Fatoye

Please initial

box

I have read the information sheet/I have had the information sheet read  
to me (delete as appropriate) and have had the opportunity to ask questions.

☐

I understand that my participation is voluntary and that I know that I am free  
to stop taking part in this study at anytime without giving any reason, without  
my legal rights being affected.

☐

I agree to participate in the above study

☐

\_\_\_\_\_  
Child's name in capital letters

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of person taking consent  
(if different from researcher)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

1 for subject and 1 for researcher

## Appendix 3.8: Ethical Approval (Queen Margaret University, Edinburgh)



Queen Margaret University College  
EDINBURGH

Francis Ade Fatoye  
Research Student  
Physiotherapy  
School of Health Sciences

Linda Welsh  
Registry Officer  
Queen Margaret University College  
Clerwood Terrace  
Edinburgh EH12 8TS

Tel: 0131 317 3219  
Email: lwelsh@qmuc.ac.uk

23 August 2004

Dear Francis Fatoye

### **Ethical Approval – Developing an assessment strategy for children diagnosed with hypermobility syndrome**

Thank you for your response dated 9 July 2004 to the letter you were sent following consideration of your application by the Research Ethics Sub-Committee.

Dr Nigel Hewlett, Convener of the Sub-Committee, has reviewed your response to the points you were required to address, and has confirmed that he is happy to take Convener's Action to grant full ethical approval for your research. He has asked that you note the following slight amendments to your Information Sheet:

- Page 1, line 1 – "Your child has **been** invited..."
- Page 3, line 25 – "the **results** of the research study..."

A standard condition of this ethical approval is that you are required to notify the Sub-Committee, in advance, of any significant proposed deviation from the protocol. Reports to the Sub-Committee are also required once the research is underway if there are any unexpected results or events that raise questions about the safety of the research. Notification of completion of the study is also required – please find the appropriate form for this enclosed.

We would like to thank you for your co-operation and wish you well with your project.

Yours sincerely

Linda Welsh  
Secretary to the Research Ethics Committee

Cc: Dr Shea Palmer, Director of Studies

Campuses at Corstorphine, Edinburgh EH12 8TS | Leith, Edinburgh EH6 8HF | Gateway Theatre, Edinburgh EH7 4AH  
Telephone +44(0)131 317 3000 Fax +44(0)131 317 3256 www.qmuc.ac.uk

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### Appendix 3.9: Ethical Permission from Edinburgh City Council



EDUCATION  
QUALITY SERVICES

Francis Fatoye  
Research Student  
QMUC  
Leith  
Edinburgh  
EH6 8HF

Date 27 May 2004

Your ref

Our ref Q/krb/rr657

Direct dial 0131 469 3164

Dear Mr Fatoye

**RESEARCH PROJECT: DEVELOPING AN ASSESSMENT STRATEGY FOR  
CHILDREN DIAGNOSED WITH HYPERMOBILITY SYNDROME**

I am writing in response to your letter dated 18 May 2004 requesting permission to undertake research in several schools in the City of Edinburgh.

Your letter has been considered and I am pleased to inform you that you have permission **in principle** to undertake your research. I must stress that it is the policy of the Education Department to leave the final decision over participation in research projects of this kind to Head Teachers and their staff. This letter does not oblige schools to take part in your research and you should make this clear to them when you make your initial approach.

I would be grateful if you could forward a copy of your completed findings to me when they become available. In this case, a summary of your findings would be acceptable. These will be of great interest to staff in the Education Department.

I would like to thank you for contacting the Education Department about your work and to wish you every success with the completion of your project.

Yours sincerely

Dr Ken Bogle  
Resources Officer



### Appendix 3.10: Letter of Invitation to the Participants (HMS Children)

NHS Lothian  
University Hospitals Division



*Royal Hospital for Sick Children - Sciennes Road - Edinburgh EH9 1LF*

Dr Janet Gardner-Medwin  
Consultant Rheumatologist

Parent of

01 July 2005

Dear Parent of

**Invitation to participate in the research study: "Developing an Assessment Strategy for Children Diagnosed with Hypermobility Syndrome (HMS)"**

We are interested in the difficulties that children have when they have flexible joints (or Hypermobility Syndrome, as it is known) and would be very grateful if you and your daughter would help us in our research. Enclosed is an information sheet which tells you all about the study that we are carrying out. You will see in it the sort of questions we would ask the children involved in this study, and you can also see how we measure the flexibility of those children's joints.

Your daughter's name has been found from the hospital records from the time she attended Dr Luqmani's rheumatology clinic at the Royal Hospital for Sick Children (RHSC), Edinburgh. This clinic visit may have been some years ago now. I have recently taken over Dr Luqmani's position, which is why you won't recognise my name.

Although I am now overseeing this research, Francis Fatoye, a physiotherapist, will be doing the study itself. He is from Queen Margaret University College, Edinburgh. This study has already had approval from the Lothian NHS Trust and Royal Hospital for Sick Children.

Your daughter's details remain confidential, and have not been given to Francis.

You are under no obligation to take part in this study. If you choose not to participate in the study it will not affect the treatment that your daughter currently receives or will receive in the future. We will only invite your daughter to take part if you return the form agreeing to learn more, or if you contact us directly.

If you think you and your daughter might like to take part in the study, please complete the form and return it in the envelope provided. If you prefer you can contact Francis by telephone or email on the numbers below. He or I will be very happy to answer any questions you have about the study before and your daughter decide whether to take part or not.

Yours sincerely

A handwritten signature in blue ink, appearing to read 'J Gardner-Medwin'.

Dr Janet Gardner-Medwin  
Senior Lecturer in Rheumatology

## **Appendix 3.11: Participant information sheet for children with HMS**



Queen Margaret University College  
EDINBURGH

### **Information Sheet for Children Diagnosed With Hypermobility Syndrome (HMS)**

#### **Study Title**

**“Developing an assessment strategy for children diagnosed with hypermobility syndrome (HMS)”**

Thank you for your interest in this study. Before you decide if you would like your child to take part it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following carefully and discuss with others if you wish. If there is anything that is not clear or you would like more information, please contact me at the number below. Take time to decide whether or not you would like your child to take part.

#### **Why has your child been chosen?**

Your child has been chosen because he/she has been diagnosed with HMS and he/she has had consultation at the Royal Hospital for Sick Children, Edinburgh, and he/she is within the ages of 8-15 years. We need to determine the level of the neuromusculoskeletal (nerves, muscles and bones) impairments and the level of the quality of life (QoL) in children diagnosed with HMS. Parents/guardians of 60 children diagnosed with HMS referred to the Royal Hospital for Sick Children, Edinburgh are being approached to allow their children to participate in this study.

#### **What is the purpose of the study?**

Joint laxity is an increase in joint range of motion beyond that which is considered normal. Hypermobility syndrome (HMS) is a generalised joint laxity with associated musculoskeletal (muscles and bones) complaints in otherwise normal subjects. Children with hypermobility syndrome (HMS) are often not diagnosed and may not receive appropriate treatment for their condition, because there is no scientific and comprehensive method of assessing the symptoms associated with their condition. The relationship between generalised joint laxity and neuromusculoskeletal (nerves, muscles and bones) complaints in children is not well understood. There is no published data on the range of neuromusculoskeletal (nerves, muscles and bones) QoL indices in children diagnosed with HMS. The relationships between symptoms and their implications for physical function and QoL are also currently unknown in children with HMS. The purpose of this study is to identify the level of impairments and the QoL associated with HMS by developing a comprehensive assessment strategy that can be used for assessment and planning of treatment.

**Do I have to allow my child to take part?**

It is up to you to decide whether or not to allow your child to take part. You do not need to give a reason if you decide not to allow your child to take part in the study. If you decide to allow your child to take part you will be given this information sheet to keep and will be asked to sign a consent form. You will also be given a copy of the consent form to keep. If you decide to allow your child to take part you are free to withdraw your child from the study at any time without giving a reason.

**What will happen to my child if I allow him/her to take part?**

Your child will report once to the QMUC human performance laboratory at Leith campus in gym short and t-shirts. A brief explanation of the procedure will be given to your child and he/she will be asked to sign a consent form. His/her weight and height will be recorded. He/she will undergo the following measurements: knee joint range of motion using a small circular device that measures joint angles, the average knee joint pain felt by your child over the last week will be assessed using a coloured scale that is like a ruler with a slide marker across it and corresponding numerical values. Your child will be instructed to slide the marker up the scale to show me how much his/her pain hurts within the last week. Knee joint position sense will be assessed using a device that moves the leg slowly and gently, muscle strength will be assessed using a small portable machine that measures the amount of force generated by a muscle or a group of muscles and functional range of motion will be assessed using a camera system whilst he/she walks. Quality of life will be assessed with a questionnaire. Both knees will be tested. The whole procedure will take approximately 1 hour.

**What does my child have to do?**

The only thing your child has to do by taking part is to report to the human performance laboratory of the Queen Margaret University College Edinburgh, and undertake the procedures outlined above.

**What are the possible disadvantages and risks of my child taking part?**

There are no possible disadvantages of your child taking part in the study as it involves non-invasive, simple and safe clinical assessments. However, there are minimal risks to your child in taking part in this study such as a possible fall or trip. Risk assessment of the human performance laboratory has been carried out to minimise these risks during your visit. However, appropriate liability insurance is in place in connection with the above mentioned study.

**What are the possible benefits of my child taking part?**

The study is not a therapeutic research project and will produce no direct benefit to your child. However, your child's participation in this research will provide the opportunity for me to identify and understand the level of the symptoms associated his/her condition (HMS). It is intended that this information will be used to develop a scientific and holistic method of assessing your child and other children with HMS, which can be used clinically to plan, and evaluate the effectiveness of any therapeutic strategy developed for children with HMS.

**What if something goes wrong?**

Your child is being asked to take part in non-invasive clinical assessments and it is unlikely that anything will go wrong. However, appropriate liability insurance is in place in connection with the above mentioned study.

**Will my child's taking part in this study be kept confidential?**

All information which is collected about your child will be kept strictly confidential. Any information about your child which leaves the premises (QMUC) will have your child's name and address removed so that you cannot recognise the child from it.

**What will happen to the results of the research study?**

The results of the research will be published some months after the study has been completed. The results will be published as research papers in medical journals and will also be available as part of research thesis at the Queen Margaret University College library. Your child will not be identified in any of the reports or medical publications and all data will only be kept until the study and all associated works are completed.

**Who is organising and funding the research?**

Francis Fatoye, a research student based at the Leith campus of the Queen Margaret University College in Edinburgh, is conducting this study. Queen Margaret University College funds the study as a PhD research degree.

**Thank you for taking the time to read this information sheet. If you or your child have any questions please do not hesitate to contact Francis Fatoye during office hours.**

Francis Fatoye MSc MCSP  
Research Student  
Physiotherapy Subject Area  
Queen Margaret University College  
89 Duke Street, Edinburgh  
EH6 8HF  
Tel: 0131 317 3665  
E-mail: [ffatoye@qmuc.ac.uk](mailto:ffatoye@qmuc.ac.uk)

INDEPENDENT CONTACT  
Dr Fiona Macmillan PhD MCSP  
Head of Physiotherapy  
Queen Margaret University College  
89 Duke Street  
Edinburgh  
EH6 8HF  
0131 317 3640  
E-mail: [fmacmillan@qmuc.ac.uk](mailto:fmacmillan@qmuc.ac.uk)



### Appendix 3.12: Parental Consent form for Children with HMS



Queen Margaret University College  
EDINBURGH

Patient's Identification Number:

#### PARENTAL CONSENT FORM (HMS CHILDREN)

**Title of Project:**

**Developing an Assessment Strategy for Children Diagnosed with  
Hypermobility Syndrome (HMS)**

**Name of Researcher:** Francis Fatoye

Please initial box

I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions.

☐

I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reason and without his/her legal rights being affected.

☐

I understand that sections of my child's medical notes may be looked at by responsible individual (Francis Fatoye). I give permission for these individuals to have access to my child's records.

☐

I agree for my child (.....) to participate in the above study

☐

\_\_\_\_\_  
Name of Child's Parent/guardian  
in capital letters

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of person taking consent  
(if different from researcher)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of Researcher

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

1 for parent/guardian and 1 for researcher

### Appendix 3.13: Participants Consent form for Children with HMS



Queen Margaret University College  
EDINBURGH

Patient's identification Number:

#### Participant Consent Form (HMS Children)

Title of Project:

***“Developing an Assessment Strategy for Children Diagnosed with  
Hypermobility Syndrome (HMS)”***

Name of Researcher: Francis Fatoye

Please initial box

I have read the information sheet/I have had the information sheet read to me (delete as appropriate) and have had the opportunity to ask questions

I know that I am free to stop taking part in this study at anytime without giving any reason and without my future care or treatment being affected.

I agree to take part in this study

\_\_\_\_\_  
Child's name in capital letters

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of person taking consent  
(if different from researcher)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of researcher

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

1 for subject and 1 for research

## Appendix 3.14: Ethical Permission (NHS Lothian Research Ethics Committees)

Lothian NHS Board

Deaconess House  
148 Pleasance  
Edinburgh  
EH8 9RS  
Telephone 0131 536 9000  
Fax 0131 536 9009  
www.nhslothian.scot.nhs.uk



Telephone: 01315369050  
Email: stephanie.butler@lhb.scot.nhs.uk  
14 February 2005

Mr Francis Fatoye  
Research Student  
Queen Margaret University College  
89 Duke Street  
Leith  
Edinburgh EH6 8HF

Dear MR Fatoye

**Full title of study:** *Developing an Assessment Strategy for Children Diagnosed with Hypermobility Syndrome (HMS)*  
**REC reference number:** 04/S1101/45

Thank you for your letter of 01 February 2005, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chairman.

### Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation [as revised].

The favourable opinion applies to the research sites listed on the attached form. Confirmation of approval for other sites listed in the application will be issued as soon as local assessors have confirmed that they have no objection.

### Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

### Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type:	Version:	Dated:	Date Received:
Application	2	11/01/2005	11/01/2005
Investigator CV	1	01/10/2004	12/10/2004
Protocol	1	01/10/2004	12/10/2004
Covering Letter		01/02/2005	08/02/2005
Summary/Synopsis	1	01/10/2004	12/10/2004
Letter from Sponsor	1	01/10/2004	12/10/2004
Compensation Arrangements	2	11/01/2005	11/01/2005
Letters of Invitation to Participants to parents	1 - to parents Jan 05	11/01/2005	11/01/2005
Letters of Invitation to Participants	1	01/10/2004	15/10/2004



GP/Consultant Information Sheets	1	01/10/2004	12/10/2004
Participant Information Sheet 2 - Feb 05 - Healthy children	2 - Feb 05 - Healthy children	01/02/2005	08/02/2005
Participant Information Sheet	1	01/10/2004	12/10/2004
Participant Consent Form	1	01/10/2004	15/10/2004
Participant Consent Form	1 - Healthy Children	11/01/2005	11/01/2005
Participant Consent Form HMS children Jan 05	2 - HMS children Jan 05	11/01/2005	11/01/2005
Response to Request for Further Information		01/02/2005	08/02/2005
Supervisor CV	1	01/10/2004	12/10/2004
Parental consent form	1	01/10/2004	12/10/2004
Parental Response Sheet	1	01/10/2004	15/10/2004
Consultant permission letter	1	01/10/2004	12/10/2004
permission for study		27/05/2004	12/10/2004
permission for study		11/06/2004	12/10/2004
Paediatric Quality of Life Report - Child	1	01/10/2004	12/10/2004
Paediatric Quality of Life Report - Teenager	1	01/10/2004	12/10/2004
Parental Consent Form Healthy children	1 Parental Consent Form Healthy Children Jan 05	11/01/2005	11/01/2005
Parental Consent Form HMS children Jan 05	2 - Parental Consent Form HMS children Jan 05	11/01/2005	11/01/2005
Letter from headteacher	1 - Letter from Headteacher Jan 05	11/01/2005	11/01/2005
correspondence with Dr Luqmaani	1 - correspondence with Dr Luqmaani	11/01/2005	11/01/2005
evidence re consultant replacing Dr Luqmaani	1 - evidence re consultant replacing Dr Luqmaani	11/01/2005	11/01/2005

#### **Management approval**

The study should not commence at any NHS site until the local Principal Investigator has obtained final management approval from the R&D Department for the relevant NHS care organisation.

#### **Membership of the Committee**

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

#### **Notification of other bodies**

The Committee Administrator will notify the research sponsor that the study has a favourable ethical opinion.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

04/S1101/45
-------------

Please quote this number on all correspondence
--

With the Committee's best wishes for the success of this project,

Yours sincerely,



**Chair**

E-mail: [stephanie.butler@lhb.scot.nhs.uk](mailto:stephanie.butler@lhb.scot.nhs.uk)

*Enclosures      List of names and professions of members who were present at the meeting and those who submitted written comments*

*Standard approval conditions*

*Site approval form (SF1)*

**Appendix 3.15: Shapiro-Wilk tests of normality for healthy children and those with HMS**

	Healthy	HMS
Pain	<0.001*	0.044*
ROM Extension	<0.000*	<b>0.210</b>
ROM Flexion	<b>0.442</b>	0.030*
Kinaesthesia	<0.001*	<0.001*
JPS at 25 degrees	<b>0.059</b>	0.019*
JPS at 10 degrees	<0.001*	<b>0.344</b>
Knee Extension Mid Stance	<b>0.859</b>	<b>0.577</b>
Loading Response	<b>0.144</b>	<b>0.774</b>
Maximum Knee Flexion	<b>0.052</b>	<b>0.085</b>
Extension muscle Torque	<b>0.701</b>	0.002*
Flexion muscle Torque	<b>0.844</b>	<0.001*

Keys: \*statistically significant at  $\alpha < 0.05$  indicating non-normal distribution for the data.

**Bold face** ( $\alpha > 0.05$  = not statistically significant) indicating normal distribution for the data.

**Appendix 4.1: Conference presentation. Physiotherapy Research Society, Scientific Conference, Nottingham, 18<sup>th</sup> April 2005.**

**AN INVESTIGATION OF THE LEARNING EFFECT OF HEALTHY SUBJECTS DURING KNEE JOINT POSITION SENSE (JPS) ASSESSMENT USING A MOTORISED DEVICE**

**F. Fatoye, S. Palmer, F. Macmillan, P. Rowe. Physiotherapy Subject Area, Queen Margaret University College, Edinburgh, UK. Email: ffatoye@qmuc.ac.uk**

**BACKGROUND:** Motorised devices have previously been used to assess knee JPS (joint position sense) (Corrigan et al. 1992; Grob et al. 2002). It is unknown, however, whether individuals' ability to accurately determine JPS changes over time. This study therefore aimed to investigate this issue.

**METHODS:** QMUC ethics committee approved the study. A convenient sample (5 adults and 5 children, age 7-31 years) participated following informed written consent (children's parents also consented). Subjects sat on an adjustable plinth with their lower leg in a padded limb support attached to a purpose-built motorised device (knee 90° flexion). The leg was passively moved by the device at a constant angular velocity of 2.2°/s to one of two different angles (25° and 10° knee flexion - the first angle tested was randomly selected). Subjects were required to press a response button as soon as the target angle was sensed. Three practice trials, where the investigator stopped the device at the target angle, were performed with the subjects' eyes open. Subjects then closed their eyes and performed five test trials, pressing the response button themselves. Once one angle was tested, the process was repeated using the remaining angle. The limb tested was selected randomly. The Absolute Angular Error (AAE) (difference between target and perceived angles) was calculated for each trial.

**RESULTS:** The mean ( $\pm$ SD) AAE changed from 5.7° (5.3) to 2.8° (5.2) and 5.6° (2.7) to 1.4° (1.8) at target angles 25° and 10°, respectively. AAE also decreased across trials in both groups at each target angle. Friedman tests revealed significant differences between trials at each target angle (both  $p < 0.001$ ). Significant differences were also found at each target angle in children (both  $p < 0.05$ ) and adults (both  $p < 0.01$ ).

**CONCLUSION:** The results suggest a learning effect using a motorised device for assessing knee JPS in healthy subjects, and researchers need to be aware of this phenomenon. The values obtained will be used in future clinical studies.

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## 275. NEUROMUSCULAR IMPAIRMENTS IN CHILDREN DIAGNOSED WITH HYPERMOBILITY SYNDROME: A PRELIMINARY STUDY

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**Background:** Impaired joint proprioception has been found in association with hypermobility syndrome (HMS) (Mallik *et al.* 1994; Hall *et al.* 1995). However, it is uncertain if other neuromuscular indices in children with HMS are impaired. Therefore, this study investigated a range of neuromuscular impairments in healthy children and those diagnosed with HMS.

**Methods:** Seventeen healthy girls (mean age 11.3±s.d. 2.5yr) and 13 girls diagnosed with HMS (mean age 11.8±s.d. 1.3yr) participated in this investigation. The study was approved by the Education Department, City of Edinburgh Council, and the QMUC and NHS Lothian Local Research Ethics Committees. Informed written consent was obtained from the participants and their parents. Knee joint kinaesthesia (KI) was assessed at 60 degrees of knee flexion and joint position sense (JPS) was examined at both 25 and 10 degrees of knee flexion using a motorised proprioception measuring device. Absolute angular error (AAE) was calculated as the difference between the target and perceived angle for JPS tests. Quadriceps and hamstrings muscle torque was measured in high sitting with the test knee in 90 degrees using a digital myometer. Muscle torque was normalised to body weight. Mann-Whitney U tests were used to compare the variables between the two groups.

**Results:** The results of this study are presented in table 1 below:

**Conclusions:** The knee joint proprioception outcome measures were significantly different in children with HMS and they also showed weaker quadriceps muscles than the healthy controls. However, there was no hamstring muscle strength deficit between the two groups. Clinicians should be aware of these identified impairments in children with HMS, and a programme of proprioception and muscle strengthening exercises may be indicated.

TABLE 1. The mean (s.d.) for joint proprioception and muscle torque

Group	Proprioception (°)			Muscle torque (Nm/kg)	
	KI at 60°	AAE at 25°	AAE at 10°	Quadriceps	Hamstrings
Healthy	1.90 (0.83)	4.56 (2.94)	2.33 (2.89)	1.49 (0.24)	0.86 (0.48)
HMS	3.15 (1.91)	7.39 (3.69)	4.92 (2.53)	1.16 (0.30)	0.63 (0.21)
P-values	0.030*	0.045*	0.011*	0.002*	0.161

\*Statistically significant at  $\alpha < 0.05$ .

## References

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## Appendix 4.3: Conference Presentation, Canadian Society for Biomechanics

### KNEE JOINT KINEMATICS AND RANGE OF MOTION IN CHILDREN DIAGNOSED WITH HYPERMOBILITY SYNDROME: A PILOT STUDY

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#### INTRODUCTION

Abnormal joint biomechanics may be a feature of hypermobility syndrome (HMS) (Grahame 1990) and the knee joint is most frequently affected by HMS symptoms (Kerr et al 2000). Computerised gait analysis in children with neuromusculoskeletal disorders is becoming popular in clinical practice and research. However, knee joint kinematics have not been reported in children diagnosed with HMS. Therefore, this study evaluated the knee joint gait kinematics, along with data for passive range of motion (ROM), in healthy children and those diagnosed with HMS.

#### METHODS

Seventeen healthy girls (mean age  $\pm$  SD = 11.3  $\pm$  2.5 years, range 8-15 years) and 13 girls diagnosed with HMS (mean age  $\pm$  SD = 12.00  $\pm$  1.5 years, range 9-15 years) participated in this study. The study was approved by the Education Department of City of Edinburgh Council, and QMUC and NHS Lothian Local Research Ethics Committees. Informed signed consent was obtained from the participants and their parents. The test knee was determined in a randomised order in healthy children, while the more painful knee was examined in children with HMS. Sagittal knee motion was recorded using a VICON motion analysis system (Oxford Metrics, England) with the participants walking at a normal self-selected speed. At least 6 trials were recorded for each subject. Passive knee ROM (flexion and extension) was measured with a universal goniometer.

Independent *t*-tests and Mann-Whitney U tests were used to compare the values between the two groups.

#### RESULTS & DISCUSSION

In Table 1 the results of the present study showed that knee flexion during loading response and maximum knee flexion during walking were significantly reduced in children with HMS when compared with healthy controls. Additionally, significantly higher values of passive knee ROM were observed in children with HMS than the controls. However, knee extension in mid stance was not statistically different between the two groups. These findings provide a basis for the usefulness of gait assessment in children diagnosed with HMS. A programme of gait re-education may be of value in children with HMS.

#### SUMMARY

Knee joint kinematics and ROM were investigated in healthy girls and those with HMS. The findings indicate that girls with HMS had lower values of sagittal knee motion during walking, with the exception of knee extension in mid stance. Girls with HMS also had higher values of passive knee ROM.

#### REFERENCES

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Table 1. The mean (SD) for sagittal knee motion, walking speed and passive knee flexion. The Median (IQR) for passive knee extension.

Group	Sagittal knee motion ( $^{\circ}$ )			Walking Speed (m/s)	Passive Knee ROM ( $^{\circ}$ )	
	KEMS	KFLR	MKF		Extension	Flexion
Healthy	2.9 (7.5)	19.8 (7.6)	61.1 (7.5)	1.0 (0.5)	-5.0 (2.0)	144.5 (3.9)
HMS	-0.4 (3.7)	13.2 (4.7)	53.8 (4.7)	1.2 (0.1)	-12.0 (3.5)	152.0 (4.5)
p-values	0.123	0.013*	0.003*	0.912	< 0.001*	< 0.001*

KEMS = knee extension in mid stance, KFLR = Knee flexion during loading response, MKF = Maximum knee flexion during swing phase. \*statistically significant at  $\alpha < 0.05$ .

## Appendix 4.4: Conference presentation, American Society of Biomechanics

### TEST-RETEST REPEATABILITY OF KINEMATICS AND RANGE OF MOTION IN CHILDREN DIAGNOSED WITH HYPERMOBILITY SYNDROME

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#### INTRODUCTION

Gait analysis and passive ROM are frequently assessed in patients with knee complaints and gait abnormalities have been observed in children with hypermobility syndrome (HMS) (Adib et al 2005). Repeatability of walking patterns has been described in healthy children (Gorton et al 1997) but not in children with HMS. Therefore, this study investigated the test-retest repeatability of knee kinematics during walking and also knee ROM measurements in both healthy children and those with HMS.

#### METHODS

Ten healthy children (mean age  $\pm$  SD =  $9.9 \pm 2.1$  years, range 8-15 years) and ten children with HMS (mean age  $\pm$  SD =  $11.8 \pm 1.3$  years, range 9-13 years) were examined. Sagittal motion during walking and passive ROM of the knee joint were assessed on two separate occasions, one week apart. The study was approved by the City of Edinburgh Council Education Department, and the QMUC and NHS Lothian Ethics Committees. Informed written consent was obtained from the participants and their parents. In healthy children the test knee was chosen at random, while the most painful knee was examined in children with HMS. Sagittal knee motion was recorded using a VICON camera

system (Oxford Metrics, England) while participants walked six times barefoot on a 7 meter walkway at their self-selected speed. Average knee joint angles were calculated for each participant. Passive knee ROM (flexion and extension) was measured with a universal goniometer. Intraclass correlation coefficient (ICC) and 95% limits of agreement (LOA) were used for data analysis.

#### RESULTS AND DISCUSSION

Tables 1 and 2 demonstrate the ICC values and 95% LOA for all the variables in healthy children and the HMS cohort respectively. Repeatability of passive ROM measurements was excellent in both groups. Based on the ICC, repeatability of KFLR in the healthy group and MKF in the HMS group was excellent. However, KEMS and MKF were measured with low to moderate repeatability in healthy children. The repeatability of KEMS and KFLR was also low to moderate in the HMS cohort. 95% LOA revealed a small variation between repeated measurements of knee passive ROM and kinematics in both groups except for MKF in healthy children. Therefore, these findings indicate good agreement between the measurement parameters except for MKF in healthy children.

Table 1. ICC and 95% limits of agreement for sagittal knee motion and passive flexion in healthy children.

	Sagittal knee motion ( $^{\circ}$ )			Passive Knee ROM ( $^{\circ}$ )	
	KEMS	KFLR	MKF	Extension	Flexion
ICC	0.74	0.84	0.48	0.95	0.96
95% LOA ( $^{\circ}$ )	-7.75 - 10.28	-6.15 - 7.59	-12.91 - 17.42	-1.07 - 1.47	-1.95 - 1.35

ICC = Intraclass correlation coefficient, KEMS = knee extension in mid stance, FLR= Knee flexion during loading response, MKF = Maximum knee flexion during swing phase, LOA = Limits of agreement.

Table 2. ICC and 95% limits of agreement for sagittal knee motion and passive knee flexion for children with HMS.

	Sagittal knee motion ( $^{\circ}$ )			Passive Knee ROM ( $^{\circ}$ )	
	KEMS	KFLR	MKF	Extension	Flexion
ICC	0.68	0.48	0.81	0.90	0.96
95% LOA ( $^{\circ}$ )	-5.74 - 7.38	-8.50 - 8.95	-4.07 - 4.86	-1.47 - 1.07	-1.38 - 1.78

ICC = Intraclass correlation coefficient, KEMS = knee extension in mid stance, FLR= Knee flexion during loading response, MKF = Maximum knee flexion during swing phase, LOA = Limits of agreement.

## SUMMARY/CONCLUSION

Between days repeatability of kinematics and passive ROM of the knee joint was investigated in healthy children and those with HMS. Based on the ICC values, this study suggests that PROM can be measured repeatedly in children using a universal goniometer while knee kinematics data (MKF in healthy children and KFLR in those with HMS) are not very repeatable. However, 95% LOA showed good agreement between repeated measurements of all the

parameters in both groups except for MKF. Therefore, the findings of the present study suggest that major clinical decisions can be based on one assessment of knee kinematics and passive ROM in children.

## REFERENCES

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**RELATIONSHIP BETWEEN KNEE KINAESTHESIA AND JOINT POSITION SENSE IN HEALTHY CHILDREN**

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**INTRODUCTION**

Joint kinaesthesia (JK) and joint position sense (JPS) are two techniques commonly used for testing proprioception of the knee joint [1]. These two proprioceptive tests have been shown to elicit different responses in the same group of subjects [2]. Moreover, in adults, lack of correlation has been observed between the two tests [3]. It is currently unknown whether, in children, similar disparities are evident in the relationship between the two techniques.

**AIM**

The aim of this study was to investigate the relationship between JK and JPS in healthy children.

**METHODS**

A convenience sample of thirty-seven healthy children (mean age  $11.5 \pm$  SD 2.6 years) participated in this investigation. The study was approved by the City of Edinburgh Council Education Department and Queen Margaret University Ethics Committee. Subjects were recruited from local schools in Edinburgh through their head teachers. Informed written consent was obtained from the participants and their parents. The knee to be tested was selected using a computer-generated random allocation. JK was assessed at  $60^\circ$  of knee flexion and JPS was examined at both  $25^\circ$  and  $10^\circ$  of knee flexion using a motorised proprioception assessment device. During JK test, subject's limb was moved at a constant angular velocity of  $0.38^\circ/\text{s}$  into extension after a random delay (between 5 to 15 seconds). During the JPS test the subject's test limb was passively moved at a constant angular velocity of  $2.2^\circ/\text{s}$  from the starting position ( $90^\circ$  of knee flexion) to the two pre-determined target angles ( $25^\circ$  and  $10^\circ$  knee flexion). JK was calculated as the threshold for passive movement (the angular displacement before the subject detected position change) while absolute angular error (AAE) was calculated as the difference between the target and perceived angles for the JPS tests. Spearman Rho Correlation analysis was used to determine the relationship between the measures of proprioception and between the JPS tests.

**RESULTS**

The findings of the Spearman Rho Correlation analysis are illustrated in Table 1. The study found a weak but statistically significant relationship between JK and JPS at  $10^\circ$ . However, non-statistically significant weak correlation was found between JK

and the JPS test at 25°. Similarly, a weak and non-statistically significant correlation was observed between the JPS tests at the two test angles.

## DISCUSSION

The findings indicate no strong correlation between JK and JPS in healthy children. Given the results of the present investigation, the findings of one proprioceptive test in children cannot be substituted for the other. Clinicians are to be aware of this as the results of independent tests of either JK or JPS may not give a full appreciation of proprioceptive acuity in children. In addition the findings of knee JPS test at one test angle may not represent the overall proprioceptive acuity in children. Therefore, these findings provide justification for continual use of both tests for knee proprioception assessment as they may be assessing two different proprioceptive systems, both of which might be important for normal function. The results of the present study also suggest that knee JPS test should not be limited to only one test angle.

## CONCLUSION

Our findings showed a weak but statistically significant correlation between JK and JPS tests at 10°. A weak and non-statistically significant correlation was found between JK and JPS tests at 25°. Similarly, a weak and non-statistically significant correlation was also observed between JPS test at these test angles. Future studies with larger sample size are required to authenticate the present findings.

## REFERENCES

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**Table 1: Spearman Correlation between proprioceptive measures**

Variables	r values	p values
JK at 60° and JPS 25°	0.150	0.374
JK at 60° and JPS at 10°	0.385	0.019*
JPS at 25° and 10°	-0.116	0.495

r = Spearman correlation coefficient; \*statistically significant at  $\alpha < 0.05$ ; JK = joint kinaesthesia; JPS = joint position sense

**Appendix 4.6: Conference presentation. Proceedings of the International Biomechanics Conference, Salford, UK. 3 – 6 September 2007**

**KNEE JOINT KINEMATICS AND RANGE OF MOTION IN CHILDREN DIAGNOSED WITH HYPERMOBILITY SYNDROME**

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**BACKGROUND**

Abnormal joint biomechanics may be a feature of hypermobility syndrome (HMS) [1] and gait abnormalities have been reported in children with this condition [2]. The knee joint is most frequently affected by the symptoms of HMS [3]. Gait assessment in children with neuromusculoskeletal disorders is becoming popular in clinical practice and research studies. A pilot study from our laboratory showed that girls with HMS walked with reduced knee flexion and increased knee extension compared with healthy girls. It is unknown if similar findings would be observed in a larger sample of both boys and girls with HMS.

**AIM**

The aim of this study was to evaluate knee joint kinematics and passive ROM (ROM) in children diagnosed with HMS and healthy controls.

**METHODS**

Twenty nine children diagnosed with HMS (21 girls and 8 boys, mean age  $\pm$  SD =  $11.9 \pm 1.8$  years, range 8-15 years) and 37 healthy children (17 girls and 20 boys, mean age  $\pm$  SD =  $11.5 \pm 2.6$  years, range 8-15 years) participated in this study. The study was approved by the Education Department, City of Edinburgh Council, the Queen Margaret University and NHS Lothian Local Research Ethics Committees. Informed written consent was obtained from the participants and their parents. A diagnosis of HMS was established using a Beighton score [4] of  $\geq 6$  in the presence of multiple joint pain (presently or historically). The knee to be tested was selected using a computer-generated random allocation in healthy children, while the more painful knee was examined in children with HMS. Sagittal knee motion and gait speed were evaluated using a VICON camera system (Oxford Metrics, England). Each subject walked 6 times barefoot on a 7m walkway. Passive knee ROM (flexion and extension) was measured with a universal goniometer (Jamar, USA). Independent t-tests were used to compare the values of sagittal knee motion and gait speed between the two groups. Mann-Whitney U tests were performed to compare passive knee ROM (flexion and extension) between the two groups.

**RESULTS**

Table 1 shows the results of knee joint angles, gait speed and passive ROM in children with HMS and the controls. The mean waveforms of knee angles in the sagittal plane during walking in the two groups are illustrated in figure 1. From Table 1, it can be seen that knee flexion during loading response (KFLR) and maximum knee flexion (MKF) during walking were significantly higher in healthy children than those with HMS. Knee extension in mid stance (KEMS) during walking was significantly higher in children with HMS than the controls. Passive ROM (extension

and flexion) was statistically higher in children with HMS than the controls. However, gait speed was not statistically different between the two groups.

## DISCUSSION

The results of the present study showed that children with HMS walked with reduced KFLR and MKF and increased KEMS when compared with healthy children. Additionally, they had higher values of passive knee ROM than healthy children. It is likely that that reduced knee flexion and increased knee extension during walking were caused by impaired knee joint proprioception, muscle weakness (quadriceps and hamstrings) and knee joint laxity that have previously been observed in individuals with HMS. These findings suggest that gait assessment might form an important component of clinical examination for children diagnosed with HMS. A programme of gait re-education and joint stability exercises may be of value to children with HMS.

## CONCLUSION

Reduced knee flexion and increased knee extension were observed during walking in children with HMS compared with healthy controls. Children with HMS also had significantly higher passive ROM than healthy children. Gait speed was not statistically different between the two groups.

## REFERENCES

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**Table 1: The mean (SD) for sagittal knee motion, gait speed and passive knee flexion.**

Group	Sagittal knee motion (°)			Gait Speed (m/s)	Passive Knee ROM (°)	
	KEMS MKF	KFLR			Extension Flexion	
Healthy	4.2 (6.0)	20.0 (6.1)	60.4 (6.6)	1.2 (0.4)	-4.0 (1.5)**	143.0 (4.5) **
HMS	-1.0 (3.5)	12.6 (4.7)	53.5 (4.6)	1.2 (0.1)	-13.0 (3.0)**	155.0 (5.5) **
P values	<0.001*	<0.001*	< 0.001*	0.496	<0.001*	< 0.001*

The Median (IQR) for passive knee extension. \*statistically significant at  $\alpha < 0.05$ .

\*\*Values are in median (IQR) and were analysed using Mann-Whitney U test. KEMS = knee extension in mid stance, KFLR = Knee flexion during loading response, MKF = Maximum knee flexion during swing phase.

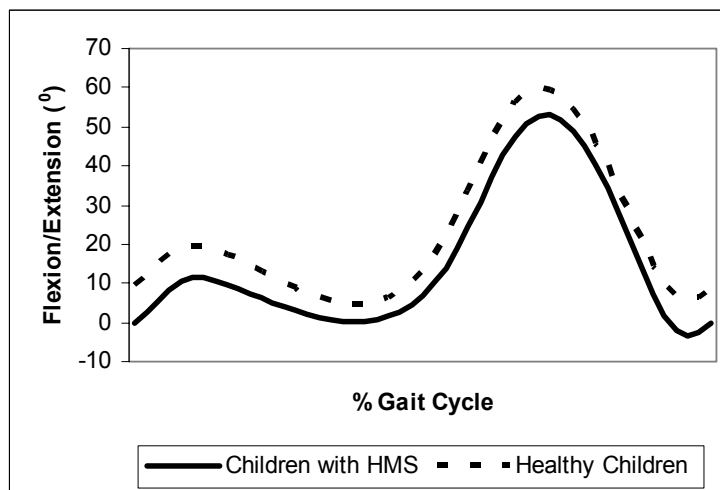


Figure 1: Sagittal knee motion during gait in healthy children and those with HMS.



**Appendix 4.7: Paper Accepted in June 2007 for Publication in Musculoskeletal Care**

**Repeatability of Joint Proprioception and Muscle Torque Assessment in Healthy Children and Children Diagnosed with Hypermobility Syndrome**

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## Abstract

**Background:** Impairment of joint proprioception in patients with hypermobility syndrome (HMS) has been well documented. Both joint proprioception and muscle torque are commonly assessed in patients with musculoskeletal complaints. It is unknown however, if these measures change significantly on repeated application in healthy children and children with HMS.

**Aim:** To investigate the between-days repeatability of joint proprioception and muscle torque in these groups.

**Methods:** Twenty children (ten healthy and ten with HMS) aged 8-15 years were assessed on two separate occasions (one week apart) for joint kinaesthesia (JK), joint position sense (JPS), and the extensor and knee flexor muscle torque of the knee. JK was measured using threshold to detection of passive movement. JPS was measured using the absolute Angular Error (AAE) (absolute difference between the target and perceived angles). Knee extensor and flexor muscle torque was normalised to body weight.

**Results:** Intra-class correlation coefficients (ICC) for JK, extensor and flexor muscle torque were excellent in both groups (range 0.83 to 0.98). However, ICC values for JPS tests were poor to moderate in the two groups (range 0.18 to 0.56). 95% limits of agreement (LOA) were narrow in both cohorts for JK and muscle torque (indicating low systematic error) but wide for the JPS tests. 95% LOA also demonstrated that the measuring instruments used in this study had low between-days systematic error.

**Conclusions:** Based on ICC and 95% LOA, the repeatability of JK and muscle torque measurements was excellent in both healthy children and those with HMS. JPS test can only be assessed with poor to moderate repeatability. The use of JPS test in these children should be undertaken with caution.

**Key words:** Joint kinaesthesia, Joint position sense, Muscle torque, Repeatability.

## Introduction

Hypermobility syndrome (HMS) is characterised by generalised joint laxity and musculoskeletal pains in the absence of systemic inflammatory joint disease such as rheumatoid arthritis (Ferrell et al., 2004). Impaired joint proprioception at the knee joint has been demonstrated in adults with HMS (Hall et al., 1994). Unpublished data from our laboratory revealed knee joint kinaesthesia (JK), joint position sense (JPS) and knee extensor muscle torque deficits in children with this condition. Early identification of neuromuscular impairments in rheumatologic patients helps in the diagnosis and establishment of appropriate treatment protocols for their conditions. However, a lack of recognisable signs makes HMS difficult to identify and manage (Ferrell et al., 2004). Children with HMS may therefore be missed during clinical assessment and may not therefore receive appropriate treatment interventions for their condition.

Impaired joint proprioception is the first neurophysiological dysfunction reported in individuals with HMS (Hall et al., 1995; Mallik et al., 1994) and has been examined using motorised devices (Hall et al., 1994; Ferrell et al., 2004). Such devices have also been used for evaluating knee joint proprioception in other clinical conditions in both children (Barrack et al., 1983b) and adults (Barrett et al., 1991; Corrigan et al., 1992; Grob et al., 2002). Similarly, the use of digital myometers for assessing muscle torque in children is becoming popular (Seniorou et al., 2002; van der Linden et al., 2004). It is a common practice for knee joint proprioception and muscle torque to be assessed together during a single session in healthy adults (Hurley et al., 1998; Rozzi et al., 1999; Ageberg et al., 2005) and those with HMS (Ferrell et al., 2004). However, the repeatability of knee joint proprioception and muscle torque assessment has not been reported in children due to a lack of previous investigative study.

There are two methods of testing joint proprioception. Firstly, joint kinaesthesia (JK) which consists of determining the threshold for perception of movement when the knee joint angle is altered slowly (less than half a degree per second) (Corrigan et al., 1992). The second method is joint position sense (JPS) and it examines the ability of a subject to reproduce an angle to which the knee joint has previously been positioned (Corrigan et al., 1992). Accurate assessment of these outcome measures would aid proper diagnosis of proprioceptive deficit in children with HMS. It would also enable the clinician to objectively determine progress and to modify any treatment plans accordingly (Thibault et al., 1994).

Studies that have investigated test-retest repeatability of knee JK and JPS have focused on adults (Barrett., 1991; Beynnon et al., 2000; Yan and Hui-Chan, 2000; Cross et al., 2005). An excellent repeatability of knee JPS has been demonstrated in healthy adults (Barrett, 1991; Yan and Hui-Chan, 2000). In addition, knee JK has been reported to be even more repeatable than JPS (Beynnon et al., 2000; Cross et al., 2005). However, to date no studies have examined the repeatability of knee JK and JPS in children. Seniorou et al., (2002) examined the test-retest repeatability of knee extensor and flexor muscle torque in healthy children and those with cerebral palsy, finding excellent repeatability in healthy children. In addition, excellent test-retest repeatability of knee extensor but low repeatability of knee flexor testing was demonstrated in children with cerebral palsy (Seniorou et al., 2002). However, no studies were found reporting the repeatability of muscle torque assessment in children with HMS.

The aim of this study was therefore to investigate the test-retest repeatability (one-week apart) of knee JPS, JK, and flexor and extensor muscle torque in healthy children and children diagnosed with HMS.

## **Methods**

### **Subjects**

Twenty children (10 healthy and 10 diagnosed with HMS) participated in this study. Mean age  $\pm$  standard deviation (SD) of the healthy controls (5 boys and 5 girls) and HMS group (2 boys and 8 girls) was  $9.9 \pm 2.1$  years (range 8-15 years) and  $11.8 \pm 1.3$  years (range 9-13 years) respectively. No subjects enrolled in the study had a history of trauma to either knee joint and vestibular system disorders. The study was approved by the City of Edinburgh Council Education Department, Queen Margaret University College Ethics Committee and National Health Service Lothian Local Research Ethics Committee. Healthy children were recruited from local schools in Edinburgh through their head teachers. Children with HMS that have attended the Rheumatology department of the Royal Hospital for Sick Children in Edinburgh were identified using the medical record system and approached for participation in the study. A diagnosis of HMS was confirmed by the first author using a Beighton score (Beighton et al., 1973) of  $\geq 6$  in the presence of multiple joint pain (presently or historically). Both parents and children gave written consent before participation in the study.

### **Testing Procedure**

To evaluate the test-retest repeatability of knee Joint Kinaesthesia (JK), Joint Position Sense (JPS), and muscle torque, each subject was tested on two separated occasions, 1 week apart. One week was chosen to minimise the possible learning effects on the part of the participants as unpublished work from our laboratory has shown within-session learning effects for JPS measurements in healthy children. This time interval was also found to be convenient for participants and their parents. Following a brief explanation of the procedure by the investigator, each subject's height and body mass were recorded. The test knee (i.e. left or right) of healthy subjects was determined in a randomised order using computer randomisation. However, the most painful knee of the children with HMS was tested. Data collection was carried out on knee JK, JPS, flexor and extensor muscle torque. To facilitate the practicalities of testing set up, the order of testing was not randomised. Testing sessions took place in the Human Motion Analysis Laboratory at QMUC Edinburgh.

### **Joint Proprioception Assessment**

Proprioception tests were carried out with a purpose-built motorised proprioception measuring device (Figure 1), with methods similar to those described by Barrack et al., (1983a), Corrigan et al., (1992) and Grob et al., (2002). The device was made up of a slow-speed motor mounted on a drive shaft, a motor control with a patient's on/off switch, an inextensible belt and a pulley attached to a the drive shaft. The inextensible belt was connected to a limb support attached to a frame that was made of a piece of aluminium rod and a protractor from which the angular displacement could be read (Figure 1). Our unpublished results demonstrated an excellent criterion-related validity (intra class correlation coefficient = 1.00) of lower leg displacement measured by this device in both healthy children and adults.

### **Joint Kinaesthesia (JK)**

JK was assessed using threshold to detection of passive movement with subjects in high sitting on an adjustable plinth with the back supported and reclined to  $60^{\circ}$  to encourage relaxation. Subjects sat with their legs hanging freely over the edge of the plinth 4-6cm proximal to the popliteal fossa (Tsang and Hui-Chan, 2003) such that the knee joint was not in contact with the plinth. This ensured that subjects' cutaneous sensation was minimised such that only the sensory receptors emanating from the test joint were being tested. The test limb was positioned such that the rotation axis of the driving shaft of the device was in line with that of the subject's test knee joint (lateral femoral condyle) and the lower leg was placed in a padded limb support (Figure 1). The starting position of the test knee was maintained at  $60^{\circ}$  of knee flexion (Grob et al., 2002) and the hips were kept at  $60^{\circ}$ . The lower leg of the test limb was strapped to the padded limb support using Velcro straps (Figure 2).

The subject's limb was then moved into extension after a random delay which varied between 5 to 15 seconds (Friden et al., 1997; Ageberg et al., 2005) at a constant angular velocity of  $0.38^{\circ}/s$ . Subjects were asked to relax and to note a clear sensation of movement or change in position of their test lower limb. Three practice trials were administered where the examiner was responsible for pressing a response button immediately the test limb started moving.

Thereafter, each subject was given the button and was instructed to press it once he/she detected position change in the test limb. Three trials were then performed by each subject. The second test trial was used as unpublished findings from our laboratory revealed that learning effects occurred during JPS tests. This phenomenon stopped after the second trial. Additionally, to standardise the protocol of assessing both JK and JPS, the same number of practice and test trials were administered for both JK and JPS tests. Visual and auditory sensory inputs were eliminated during the trials by means of blindfold and earmuffs respectively (Skinner et al., 1986; MacDonald et al., 1996). The angular displacement of the knee joint (before the subject detected position change) for the second trial was recorded in degrees as the threshold response for the subject.

### **Knee Joint Position Sense (JPS)**

JPS testing can be performed under either weight-bearing or non weight-bearing conditions. The former condition has the advantage of providing proprioceptive data under a more functional condition (Bullock-Saxton et al., 2001) that is clinically relevant, but it involves both motor and sensory receptors (Barrett et al., 1991). To minimise the possible motor involvement and its contribution to JPS in the weight-bearing method, passive JPS tests were used for this study. This ensured that proprioceptive input emanated from the test joint and not from the muscles acting on the knee joint. The experimental set up and subjects' position was identical to that of JK above (Figure 2), except that the starting position of the test knee was  $90^{\circ}$  flexion (Grob et al., 2002).

The motorised device passively moved the subject's test limb from the starting position ( $90^{\circ}$  of knee flexion) to two pre-determined target angles ( $25^{\circ}$  and  $10^{\circ}$  knee flexion), at an angular velocity of  $2.2^{\circ}/s$ . Three practice followed by three test trials were administered for both test angles. To enable the subject to remember the target positions, the test limb was held in these angles for approximately 10 seconds (Callaghan et al., 2002) during the practice trials. Subjects were asked to

concentrate on the position. The leg was then returned to the starting position using the motor, where it was left for 15 seconds (Corrigan et al., 1992).

Each subject was instructed to relax during the testing and was told to press the response button when he/she thought that the limb had reached the target position previously demonstrated. The absolute angular error (AAE) (the absolute difference between target and perceived angle at each test angle was calculated).

### **Muscle Torque**

Knee extensor and flexor muscle torque was quantified using a digital myometer (MIE, Medical Research Ltd, England). Subjects sat on a plinth with their back supported and reclined to 60° and the test knee flexed to 90° (Figure 3). A non-extensible myometer strap was strapped around the lower leg 5cm proximal to the base of the malleoli of the subjects' test limb and the other end was attached to one side of the transducer body of the myometer. Another non-extensible strap was attached to the frame of the plinth (underneath the subject) and to the other side of the myometer transducer and with the straps perpendicular to the limit. Extensor muscle torque was measured first by instructing the subjects to straighten their knees from the starting position (Clarkson, 2000). Flexor muscle torque was then assessed with the subjects in the same position and the same experimental set up and procedure except that the myometer strap was attached to an a fixed plinth positioned in front of the subject and they were instructed to bend the test knee as much as possible. Subjects were given consistent verbal instruction and encouragement. The maximum contraction produced once by the extensors and flexors displayed as force on the myometer was recorded in Newtons (N). Knee extensor and flexor muscle torque was calculated in Newton meters (Nm) for each subject as the product of force and the perpendicular distance between the lateral femoral condyle and the myometer strap measured using a tape measure. Muscle torque was then normalised to body mass (Nm/kg).

### **Data Analysis:**

Two measurements of repeatability were calculated - Intra class correlation coefficient (ICC 1, 1) and Bland and Altman limits of agreement (Rankin and Stoke, 1998). Bland and Altman plots were generated to show the relationship between the differences in the first and the second measurements and their mean with 95% limits of agreement (mean difference between the two measurements  $\pm$  2 standard deviations) (Bland and Altman, 1986).

### **Results**

Tables 1 (healthy children) and 2 (HMS children) present the mean and standard deviations (SD) attained in sessions 1 and 2. The intra class correlation coefficient (ICC), mean differences and 95% limits of agreement (LOA) values of all measurements in healthy children and those with HMS are also displayed in these tables. Figures 4 and 5 show the Bland and Altman plots for the HMS group.

The ICC values for joint kinaesthesia (JK) and muscle torque in healthy controls and the HMS group were high (0.83 - 0.97) indicating excellent repeatability. However, the ICC values for joint position sense (JPS) measurements ranged from poor to moderate in both groups (0.18 – 0.56). There were small mean differences in JK and JPS (range = -0.11° to 1.9°), and knee extensor and flexor torque (range = -0.02 to 0.03Nm/kg) in both healthy children and the HMS group.

Figure 4a, b and c illustrate the Bland and Altman plots for JK and JPS at 25° and 10° of knee flexion for the HMS group. From the figure, it can be seen that all measurements but one were within 95% LOA for the three proprioceptive outcome measures.

95% LOA revealed an excellent agreement of (1.24° to 1.04°) for knee JK in healthy children and in children with HMS (-1.82° to 2.42°). However, a poor agreement was recorded for JPS at 25° (-3.43 to 6.23°) and at 10° (-4.27 to 7.07°) of knee flexion respectively in healthy children. Similarly, a poor agreement was also observed for JPS at 25° (-10.76° to 10.16°) and at 10° (-5.96 to 9.76°) in the HMS group. It was noticed that JK and JPS at both 25° and 10° were higher in the HMS group than the healthy cohort. JPS also decreased during the second measurement sessions in both groups.

Figure 5a and b demonstrate the Bland and Altman plots for the knee extensors and flexors muscle torque in the HMS cohort. 95% LOA displayed in Tables 1 and 2 demonstrate an excellent agreement between the two measurement sessions in healthy children for the extensor (-0.12 to 0.07 Nm/kg) and knee flexor muscle torque (-0.13 to 0.10 Nm/kg). The agreement in the HMS group ranged from 0.30 to 0.37 and -0.07 to 0.08 Nm/kg for knee extensors and flexors respectively. The small ranges in LOA recorded in the two groups indicate excellent repeatability in knee muscle torque testing in the two cohorts. Both extensor and flexor muscle torque values were higher in the control group than the HMS cohort.

Extensor muscle torque was higher than flexor muscle torque in both groups. Analysis of the combined data (healthy and HMS cohorts) for the two JPS tests revealed that the ICC values for the combined group increased (ICC range = 0.26 to 0.58) for both JPS tests. However, this increase did not reach the acceptable ICC value of 0.80 indicating poor repeatability of JPS measures. A paired t-test revealed no significant differences (p values range = 0.100 to 0.860) between repeated measurements of JPS at both target angles in the each group indicating that no detectable learning effect occurred between the measurements (one week apart).

### Discussion

This study investigated the test-retest repeatability of knee joint proprioception and muscle torque assessments in healthy children and those with HMS. Our findings demonstrated that knee joint kinaesthesia (JK) and muscle torque could be measured with high repeatability in healthy children and those with HMS while joint position sense (JPS) tests can only be assessed with poor to moderate repeatability in these children. The investigation also showed that these measurement parameters have low between-days systematic differences. These findings suggest that, using these assessments, clinicians could reliably measure JK and muscle torque in children diagnosed with HMS. Such assessments could be used to identify impairments and changes over time, thereby influencing treatment plans for children with this condition.

No previously published study has been found investigating knee JK and JPS in children. Therefore, the findings of this study were examined in relation to those reported in adults. Our results agree with the study of Beynnon et al., (2000) and Yan and Hui-Chan, (2000) who found excellent test-retest repeatability of knee JK in adults. In addition, the current study demonstrated that JK measurements were more repeatable than JPS tests, with only poor to moderate JPS repeatability in

both groups. These findings confirm the results reported by Beynnon et al., (2000) and Cross et al., (2005) for healthy adults.

On the other hand, the low repeatability of JPS tests ( $ICC = 0.18-0.56$ ) obtained in the present study contrasts with the results of Tsang and Hui-Chan (2003). They found between-days (1 week apart) repeatability of passive JPS to be excellent ( $ICC = 0.90$ ) in eleven healthy elderly subjects (mean age  $\pm$  SD =  $70.8 \pm 4.0$  yrs). There are a few potential reasons for this discrepancy. In the study by Tsang and Hui-Chan, (2003), subjects were tested in sitting with the knee at a starting angle of  $30^{\circ}$  and target angle of  $3^{\circ}$  flexion. Whereas, in our study the starting knee angle was  $90^{\circ}$  and the target angle were  $25^{\circ}$  and  $10^{\circ}$  flexion.

It has been reported that joint mechanoreceptors are more sensitive near end range of knee extension (Lephart et al., 1992; Borsa et al., 1997). Since the target angle of the knee joint used in Tsang and Hui-Chan's study was closer to the end range of knee extension than in the present investigation, it is possible that the knee joint mechanoreceptors in their subjects were somewhat more activated. Therefore, our results on JPS could have been due to the target angles of the knee joint. The low repeatability of JPS measurements in the present study could be due to the participants' age. It has been found that proprioceptive acuity decreases with an increase in age in adults (Skinner et al., 1984; Hurley et al., 1998) but increases with advancing age in children (Visser and Geuze, 2001; Goble et al., 2005). Growth spurts in children are believed to be accompanied by stretching of the collagen (Bird, 2005) and this may therefore cause a temporary proprioception deficit in children compared with adults. Cutaneous input was eliminated by means of an air splint in the study by Tsang and Hui-Chan, (2003). However, cutaneous input was not eliminated in the present study by means of an air splint. It is believed that air splints, in addition to eliminating cutaneous sensation may stimulate articular mechanoreceptors (Stillman, 2000). Again, the findings of Tsang and Hui-Chan, (2003) could be the result of the air splint used as this could also have enhanced the proprioceptive accuracy of their participants and may have resulted in the better test-retest repeatability reported in their study.

Our findings on knee muscle torque confirm the findings of Seniorou et al., (2002) who observed an excellent test-retest repeatability of knee extensors in healthy children ( $ICC = 0.93$ ) and children with cerebral palsy ( $ICC = 0.79$ ) using a digital myometer. It is difficult to make detailed comparison between the results of the present study with that previous investigation due to differences in subjects' characteristics. The combined data within the present study (healthy children and those with HMS) was analysed to examine if the low ICC values obtained for the JPS tests were due to the small range of the data in either group. The ICC value of the combined analysis did not reach the acceptable value of 0.80 confirming the poor to moderate repeatability of JPS tests observed in the two groups. It was anticipated that repeatability of knee joint proprioception and muscle torque assessment was going to be poorer in children with HMS than the controls. However, our findings were similar in both groups. It has been reported that joint proprioception acuity (Goble et al., 2005) and muscle torque (Eek et al., 2006) improved with age in children. Therefore, the possible reason for this observation could be that the HMS group were a little older than the controls. This factor could have enhanced proprioceptive acuity and muscle performance in children with HMS.



The mean absolute angular error (AAE) for both JPS at 25° and 10° decreased during the second session in both healthy children (Tables 1) and those with HMS (Table 2), suggesting that learning effects might have been a factor. These decreases were not statistically significant, however (paired t-test p range = 0.100 to 0.860). The higher JK and JPS values obtained in children with HMS suggest impaired joint proprioception (Hall et al., 1995; Mallik et al., 1994). Similarly, the higher muscle torque recorded in the control group could signify muscle weakness in children with HMS. Such differences were not specifically investigated in the current study, and require statistical verification in future research with a larger sample size. Such an investigation is currently ongoing at this centre.

There are some limitations to this study. First, only the knee joint was tested in the present study thereby limiting the generalisability of our findings to other joints. Secondly, the participants in the present study were healthy children and those with HMS. Therefore, the findings should be extrapolated to other groups with caution. Additionally, the limited number of participants in this study may have contributed to false negative findings (Type 2 errors) in relation to JPS. The findings do, however, provide important preliminary data on the test-retest repeatability of knee joint proprioception and muscle torque in children with HMS.

In summary, this study showed that knee JK and muscle torque assessments are repeatable in both healthy children and children with HMS, while JPS tests can only be examined with poor to moderate repeatability. Therefore, on the basis of these findings, JPS tests in children should be used with caution.

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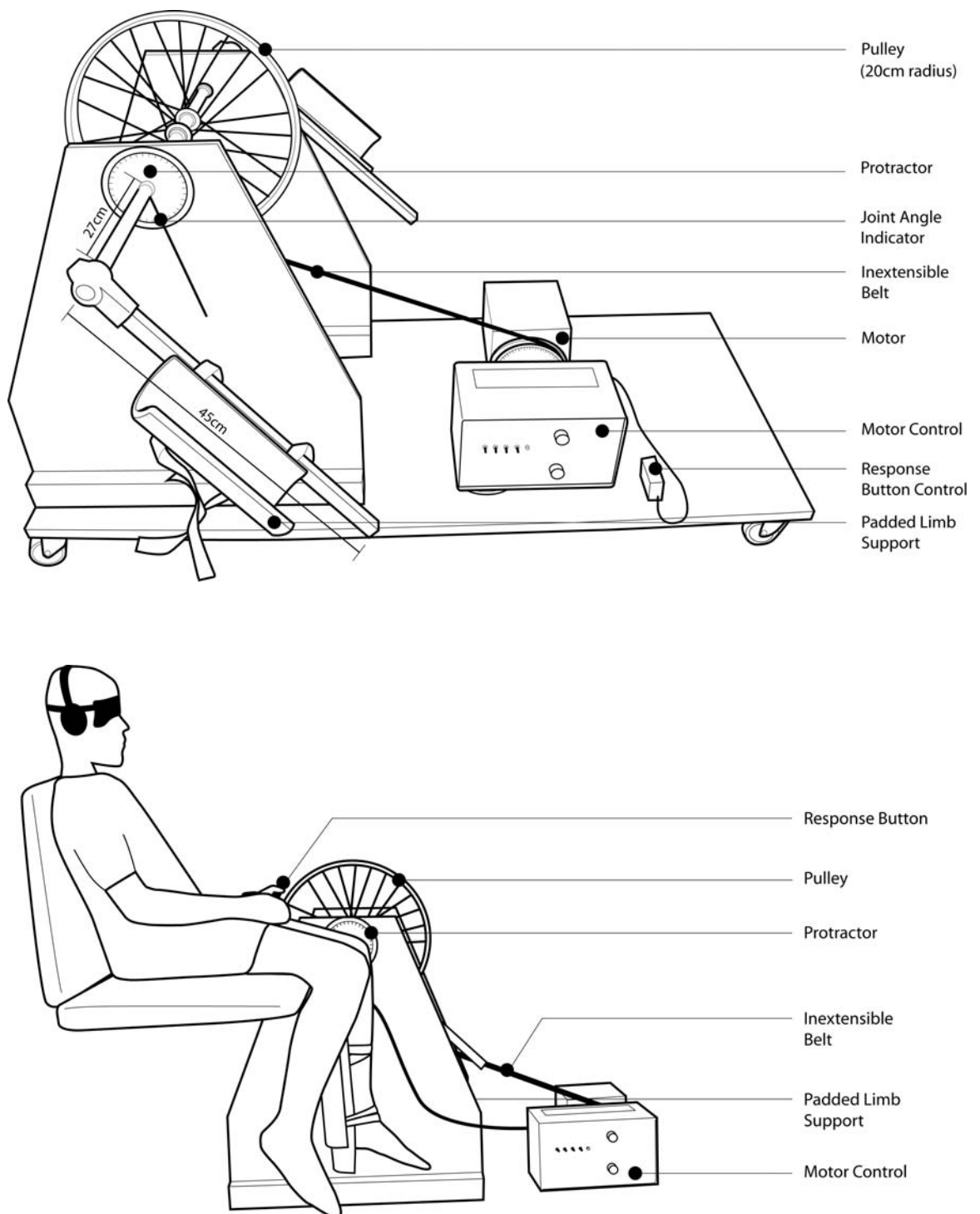


Figure 2: Experimental set-up showing the starting position for knee joint position sense testing

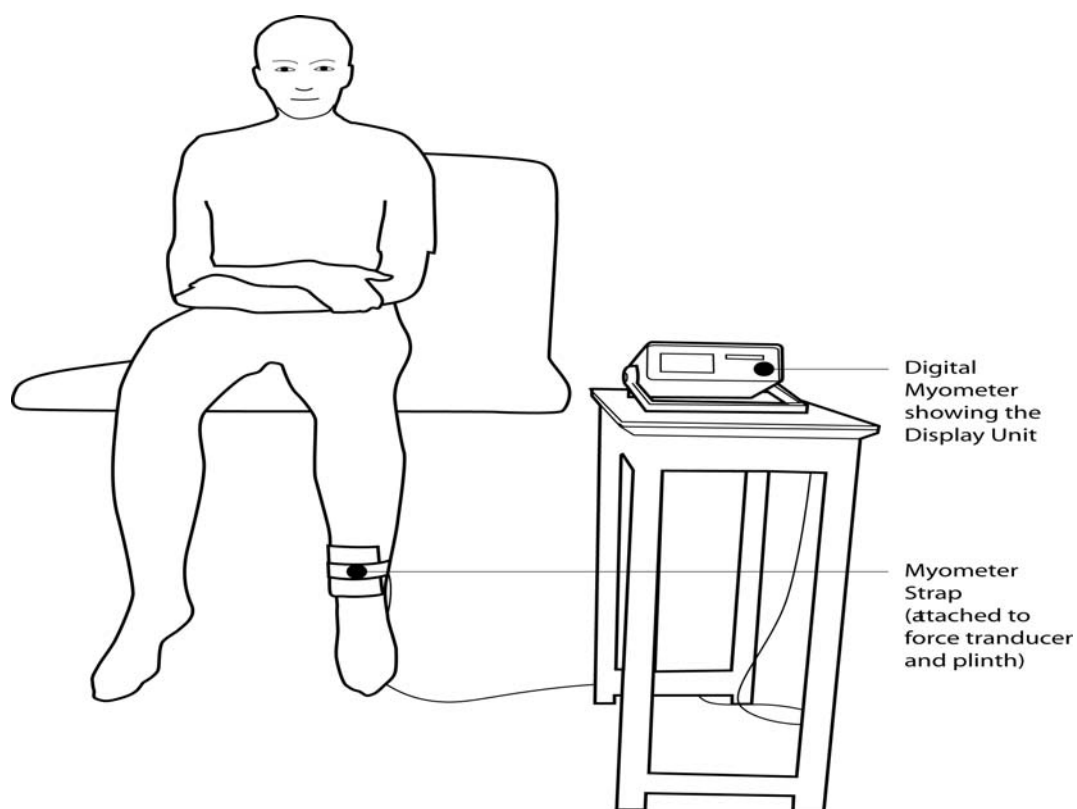


Figure 3: Subject's position for testing knee extensor muscle torque

Table 1: Results of between-days repeatability in healthy children: Mean (SD = standard deviation), ICC = Intraclass correlation coefficients.

	Day 1	Day 2	ICC	Mean Difference	95% Limits of Agreement
JK ( $^{\circ}$ )	2.00 (0.81)	1.90 (1.10)	0.83	-0.11	-1.24 to 1.04
JPS at 25 ( $^{\circ}$ )	4.00 (2.67)	2.60 (2.01)	0.39	1.40	-3.43 to 6.23
JPS at 10 ( $^{\circ}$ )	2.80 (3.25)	1.40 (1.07)	0.26	1.40	-4.27 to 7.07
Muscle Torque Extensors (Nm/kg)	1.37 (0.24)	1.39 (0.25)	0.98	-0.02	-0.12 to 0.07
Muscle Torque Flexors (Nm/kg)	0.73 (0.18)	0.74 (0.17)	0.95	-0.01	-0.13 to 0.10

Table 2: Results of between-days repeatability in children with HMS: Mean (SD= standard deviation), ICC = Intraclass correlation coefficients.

	Day 1	Day 2	ICC	Mean Difference	95% Limits of Agreement
JK ( $^{\circ}$ )	3.00 (2.16)	2.70 (1.57)	0.84	0.3	-1.82 to 2.42
JPS at 25 ( $^{\circ}$ )	6.60 (3.92)	6.30 (5.59)	0.56	0.3	-10.76 to 10.16
JPS at 10 ( $^{\circ}$ )	4.90 (3.67)	3.00 (2.63)	0.18	1.9	-5.96 to 9.76
Muscle Torque Extensors (Nm/kg)	1.30 (0.33)	1.27 (0.27)	0.85	0.03	-0.30 to 0.37
Muscle Torque Flexors (Nm/kg)	0.67 (0.17)	0.67 (0.14)	0.97	0.01	-0.07 to 0.08

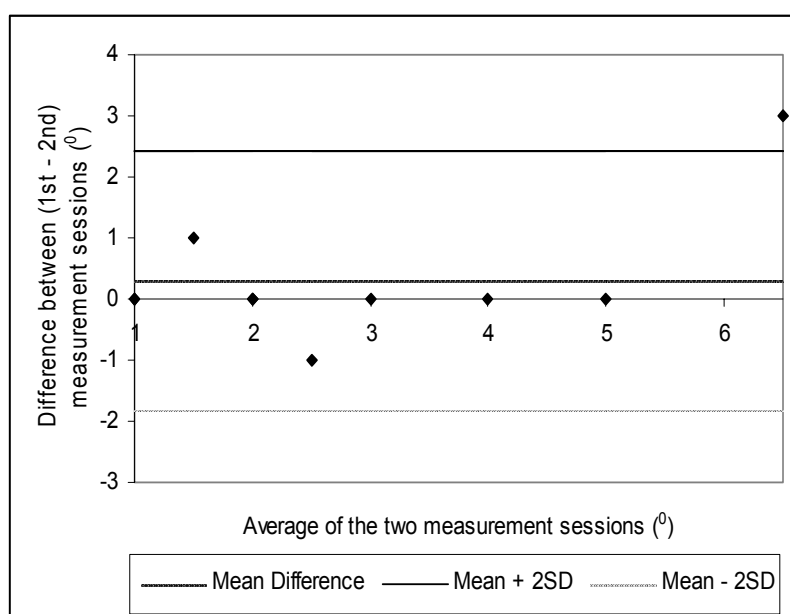


Figure 4a: Kinaesthesia (JK) in the HMS Cohort (n = 10).

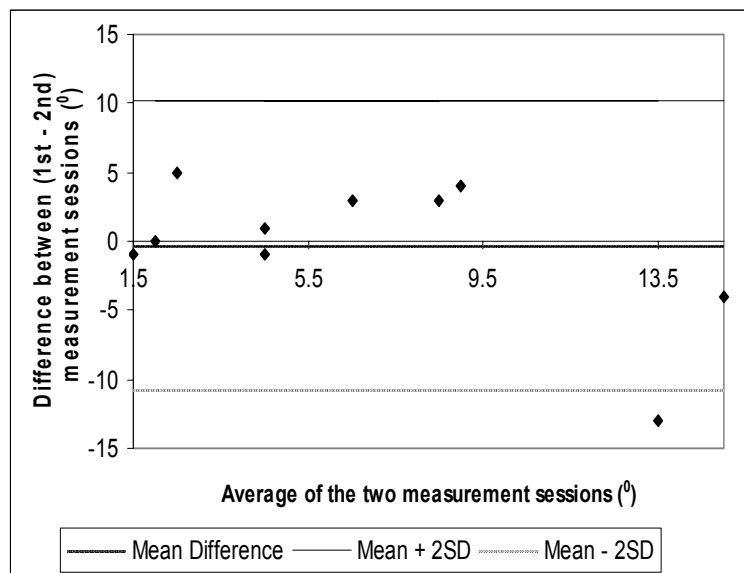


Figure 4b: JPS at 25 degrees in the HMS group (n = 10).

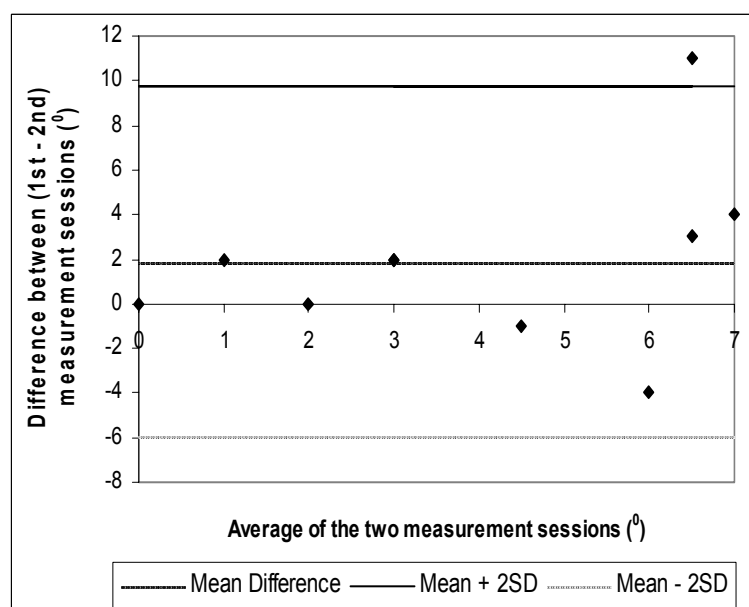


Figure 4c: JPS at 10 degrees in children with HMS (n = 10).

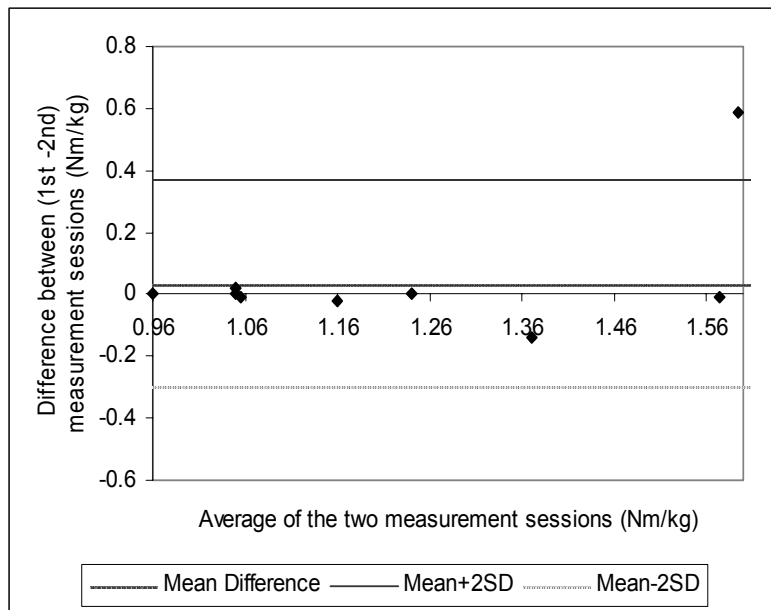


Figure 5a: Knee extensor muscle torque in the HMS Cohort (n = 10).

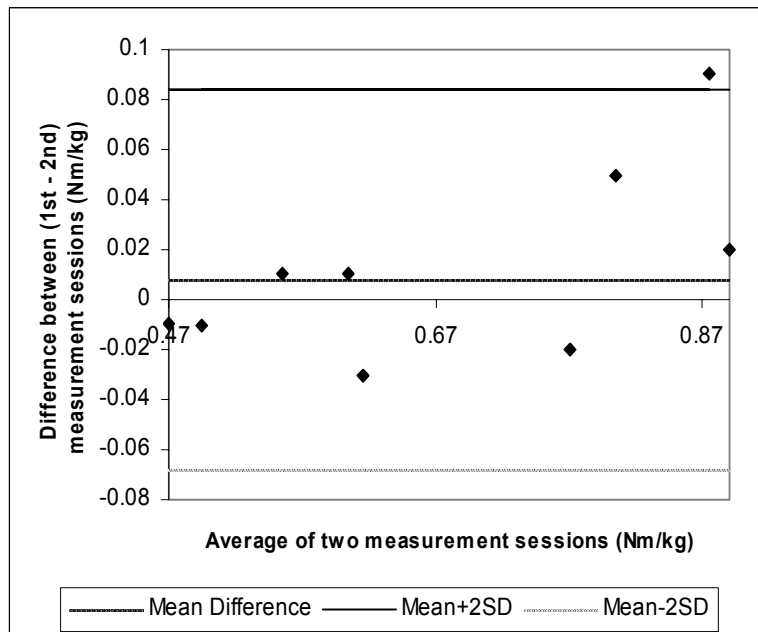


Figure 5b: Knee flexor muscle torque in the HMS group (n = 10).



## PAIN AND QUALITY OF LIFE PERCEPTION IN CHILDREN WITH HYPERMOBILITY SYNDROME

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**Background:** Hypermobility syndrome (HMS) is a major source of morbidity in children. Due to pain, activities of daily living, physical and sports activities may be limited in children with HMS (Murray and Woo 2001). However, this has not been well documented. Ruperto et al. (2004) reported that functional ability and physical and psychosocial well-being of children with generalised joint laxity were not affected when compared with healthy controls. Their study was conducted on children with generalised joint laxity, however, and not those with HMS. Therefore, it is currently unclear whether quality of life (QoL) in children with HMS is affected. This study compared pain and QoL in children diagnosed with HMS with healthy controls.

**Methods:** Sixty-six children (29 diagnosed with HMS and 37 healthy children) aged 8-15 years participated in this study. Ethical approval was obtained for the study. Informed written consent was obtained from the participants and their parents/guardians. A diagnosis of HMS was established using the Beighton criteria (Beighton et al. 1973). The test knee was determined in healthy children using computer randomisation, while the more painful knee was examined in children with HMS. Average knee joint pain over the past week was examined using the Coloured Analogue Scale. QoL was measured via the Pediatric Quality of Life Inventory. Mann-Whitney U tests were performed to compare pain and QoL scores between the two groups.

**Results:** The results of this study are presented in Table 1.

**Conclusions:** The findings of the present study showed that children with HMS had significantly higher pain perception and poorer QoL when compared with healthy children. Each of the domains of QoL was also significantly poorer in children with HMS than healthy children. Pain and QoL assessment might form important components of clinical examination for children diagnosed with HMS. Appropriate treatment programmes to alleviate pain and improve QoL in children with HMS should be developed.

### References

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Table 1: The median (IQR) for pain and QoL measures

Group	Pain	Physical	Emotional	Social	School	Overall
Healthy	0.0 (0.0)	100.0 (3.1)	100.0 (10.0)	100.0 (5.0)	100.0 (0.0)	100.0 (6.8)
HMS	2.5 (5.3)	75.1 (26.6)	90.0 (27.5)	90.0(25.0)	90.0 (45.0)	82.6 (21.8)
P values	<0.001*	<0.001*	0.003*	<0.001*	0.008*	<0.001*

QoL domains: Physical = physical functioning; emotional = emotional functioning; social = social functioning; school = school functioning; overall = overall QoL.

\*statistically significant at  $p < 0.05$ .

**LACK OF CORRELATION BETWEEN KNEE JOINT KINAESTHESIA AND POSITION SENSE TESTS IN CHILDREN WITH HYPERMOBILITY SYNDROME**

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**BACKGROUND**

Hypermobility syndrome (HMS) is diagnosed when generalised joint laxity is associated with musculoskeletal complaints (Ferrell et al. 2004). Impaired knee joint proprioception has been found in individuals with HMS. Joint kinaesthesia (JK) and joint position sense (JPS) techniques have been used for testing knee joint proprioception in healthy children and those with HMS. These two proprioceptive tests have shown to elicit different responses in a group of adults with a knee problem. Moreover, a preliminary investigation at our department revealed a lack of correlation between the two tests in healthy children. It is currently unknown whether, in children with HMS, similar disparities are evident.

**PURPOSE OF STUDY**

The aim of this study was to investigate the relationship between JK and JPS in children with HMS.

**RELEVANCE OF STUDY**

The present study will help to determine whether these two proprioceptive tests can be used interchangeably and/or if one test reflects the overall proprioceptive ability in children with this condition.

**PARTICIPANTS**

Twenty nine children diagnosed with HMS (21 girls and 8 boys, mean age (SD) = 11.9 (1.8) years, range 8-15 years) participated in this investigation.

**METHODS**

Participants were recruited from a rheumatology department and podiatry clinic in Edinburgh. Their parents were approached by the consultant rheumatologist and/or the head of podiatry. Informed written consent was obtained from the participants and their parents/guardians. A diagnosis of HMS was established using the Beighton criteria (Beighton et al. 1973). The more painful knee (as reported by the children) was examined. Knee JK was assessed at 60° of knee flexion and JPS was examined at both 25° and 10° of knee flexion using a motorised proprioception assessment device. JK was calculated as the threshold for detection of passive movement while absolute angular error (AAE) was calculated as the difference between the target and perceived angles for JPS tests.

**ANALYSIS**

Spearman Rho Correlation analysis was used to determine the relationship between the two measures of proprioception. Statistical significant was set at  $p \leq 0.05$ .

**RESULTS**

The findings of this study demonstrated no relationship between JK and the two JPS test at 25° ( $r = 0.004$ ;  $p = 0.984$ ). No correlation was also found between JK and JPS at 10° ( $r = -0.158$ ;  $p = 0.413$ ). In addition, no relationship was observed between JPS test at both test angles ( $r = 0.136$ ;  $p = 0.482$ ).

**CONCLUSION**

The findings indicated that one proprioceptive test in children with HMS should not be substituted for the other. Therefore, both tests should be used for knee proprioception assessment to determine the overall proprioceptive function in children with this condition. Clinicians are to be aware of this and should not make clinical judgement based on independent test of either JK or JPS.

**IMPLICATIONS**

The results of this study imply that JK and JPS may be assessing two different aspects of proprioception, both of which might be impaired in children with HMS.

**REFERENCE**

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**KEY WORDS**

Proprioception, hypermobility syndrome, children